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Synthetic enzymes for the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin and vanillic acid and their use

The present invention relates to <u>synthetic enzymes</u> for the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin and vanillic acid, the use thereof for the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin and vanillic acid, DNA coding for the aforementioned enzymes and microorganisms transformed therewith.

The first article relating to the degradation of eugenol was written by Tadasa in 1977 (Degradation of eugenol by a microorganism. Agric. Biol. Chem. 41, 925-929). It describes the degradation of eugenol with a soil isolate which was presumed to be <u>Corynebacterium</u> sp. In this process ferulic acid and vanillin were identified as intermediate degradation products and the subsequent degradation was assumed to proceed via vanillic acid and protocatechuic acid.

In 1983 another article by Tadasa and Kyahara appeared (Initial Steps of Eugenol Degradation Pathway of a Microorganism. Agric. Biol. Chem. 47, 2639-2640) on the initial steps of eugenol degradation, this time with a soil isolate which was identified to be <u>Pseudomonas</u> sp. In this article eugenol oxide, coniferyl alcohol and coniferylaldehyde were described as intermediates for the formation of ferulic acid.

Also in 1983 a report by Sutherland et al. appeared (Metabolism of cinnamic, p-coumaric, and ferulic acids by Streptomyces setonii. Can. J. Microbiol. 29, 1253-1257) on the metabolism of cinnamic, p-coumaric and ferulic acids by Streptomyces setonii. In this process ferulic acid was degraded via vanillin, vanillic acid and protocatechuic acid, the ring-cleaving enzymes catechol 1,2-dioxygenase and protocatechuate 3,4-dioxygenase having been indirectly identified in the cell-free extract.

In 1985 Ötük (Degradation of Ferulic Acid by Escherichia coli. J. Ferment. Technol. 63, 501-506) reported on the degradation of ferulic acid by a strain of Escherichia coli isolated from decaying bark. Here as well vanillin, vanillic acid and protocatechuic acid were found as degradation products.

X i. e. Synthesis enzymes

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isoeugenol) for the microbial oxidation of eugenol and isoeugenol. However, only when isoeugenol was used the process did produce high conversion rates; the results were very poor using eugenol.

In 1991 EP-A 453 368 appeared ["Production de vanilline par bioconversion de précurseurs benzeniques" (Production of vanillin by the bioconversion of benzene precursors)], in which the reaction to form vanillin from vanillic acid and ferulic acid using a basidiomycete - <u>Pycnoporus cinnabarinus</u> CNCM I-937 and I-938 - was observed.

In 1992 the Takasago Perfumery Company was granted a Japanese patent (Preparation of vanillin, coniferyl-alcohol and -aldehyde, ferulic acid and vanillyl alcohol - by culturing mutant belonging to <u>Pseudomonas</u> genus in presence of eugenol which is oxidatively decomposed; JP 05 227 980 21.1.1992) for the preparation of vanillin, coniferyl alcohol, coniferylaldehyde, ferulic acid and vanillyl alcohol from eugenol using a <u>Pseudomonas</u> mutant.

Also in 1992 US Patent No. 5,128,253 by Labuda et al. (Kraft General Foods) (Bioconversion process for the production of vanillin) was granted, in which a biotransformation process for the production of vanillin was described. Here as well the starting material was ferulic acid and the organisms used were Aspergillus niger, Rhodotorula glutinis and Corynebacterium glutamicum. The crucial feature was the use of sulphydryl components (e.g. dithiothreitol) in the medium. In 1993 the subject matter of the patent also appeared in the form of a publication (Microbial bioconversion process for the production of vanillin; Prog. Flavour Precursor Stud. Proc. Int. Conf. 1992, 477-482).

EP-A 542 348 (Process for the preparation of phenylaldehydes) describes a process for the preparation of phenylaldehydes in the presence of the enzyme lipoxygenase. Eugenol and isoeugenol are for example used as substrates. We have attempted to rework the process using eugenol, but have not succeeded in confirming the results of the reactions.

DE-A 4 227 076 [Verfahren zur Herstellung substitutierter Methoxyphenole und dafür geeigneter Mikroorganismus (Process for the production of substituted methoxyphenols and a microorganism suitable for said process)] describes the production of substituted methoxyphenols with a new <u>Pseudomonas</u> sp. The

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starting material used is eugenol and the products are ferulic acid, vanillic acid, coniferyl alcohol and coniferylaldehyde.

Also in 1995 a comprehensive review by Rosazza et al. (Biocatalytic transformation of ferulic acid: an abundant aromatic natural product; J. Ind. Microbiol. <u>15</u>, 457-471) appeared on possible methods of biotransformation using ferulic acid.

The present invention relates to synthetic enzymes for the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin and vanillic acid from eugenol.

Synthetic enzymes according to the invention are for example:

- a) eugenol hydroxylase,
- b) coniferyl alcohol dehydrogenase,
- c) coniferylaldehyde dehydrogenase,
- d) ferulic acid deacylase and
- e) vanillin dehydrogenase.

The invention also relates to DNA coding for the abovementioned enzymes and cosmid clones containing this DNA as well as vectors containing this DNA and microorganisms transformed with the DNA or the vectors. It also relates to the use of the DNA for the transformation of microorganisms for the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin and vanillic acid. The invention also relates to partial sequences of the DNA and functional equivalents. Functional equivalents are understood to be those derivatives in which individual nucleobases have been substituted (wobble substitutions) without resulting in any functional changes. In relation to proteins, amino acids can also be substituted without resulting in any functional changes.

The invention also relates to the individual steps for the production of coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin and vanillic acid from eugenol, i.e. in concrete terms:

a) the process for the production of coniferyl alcohol from eugenol carried out in the presence of eugenol hydroxylase;

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- b) the process for the production of coniferylaldehyde from coniferyl alcohol carried out in the presence of coniferyl alcohol dehydrogenase;
- c) the process for the production of ferulic acid from coniferylaldehyde carried out in the presence of coniferylaldehyde dehydrogenase;
- 5 d) the process for the production of vanillin from ferulic acid carried out in the presence of ferulic acid deacylase;
 - e) the process for the production of vanillic acid from vanillin carried out in the presence of vanillin dehydrogenase.

After NMG mutagenesis mutants with defects in individual stages of the catabolism of eugenol were obtained from the eugenol-utilising <u>Pseudomonas</u> sp. strain HR 199 (DSM 7063). Using total DNA of wild-type <u>Pseudomonas</u> sp. HR 199 partially digested with <u>Eco</u>RI a gene library was constructed in the pVK100 cosmid, which has a broad host spectrum and can also be replicated in stable form in pseudomonads. After packaging in 1-phage particles the hybrid cosmids were transduced to <u>E. coli</u> S17-1. The gene library comprised 1330 recombinant <u>E. coli</u> S17-1 clones. The hybrid cosmid of each clone was transferred by conjugation into two eugenol-negative mutants (mutants 6164 and 6165) of the <u>Pseudomonas</u> sp. HR 199 strain and tested for a possible capacity for complementation. In this test two hybrid cosmids (pE207 and pE115) were identified, the obtainment of which restored mutant 6165's capacity to utilise eugenol. One hybrid cosmid (pE5-1) resulted in the complementation of mutant 6164.

The complementing capacity of plasmids pE207 and pE115 was attributed to a 23 kbp EcoRI fragment (E230). A physical map of this fragment was prepared and the fragment completely sequenced. The genes vanA and vanB which code for vanillate demethylase were localised in a 11.2 kbp HindIII subfragment (H110). Another open reading frame (ORF) was found to be homologous to g-glutamyl cysteine synthetase produced by Escherichia coli. An additional ORF, which was homologous to formaldehyde dehydrogenases, was identified between the aforementioned ORF and the vanB gene. Two additional ORF's were found to be homologous to the cytochrome C subunit or the flavoprotein subunit of p-cresol methylhydroxylase, respectively produced by Pseudomonas putida. In the Pseudomonas sp. HR 199 strain, these ORF's code for a new not previously

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described eugenol hydroxylase which converts eugenol into coniferyl alcohol via a quinone methide derivative by a process analogous to the reaction mechanism of p-cresol methyl hydroxylase. Another ORF of an unknown function was identified between the genes of the two subunits of eugenol hydroxylase. An ORF which was homologous to lignostilbene-a,b-dioxygenase was identified in a 5.0 kbp HindIII subfragment (H50). In addition one ORF was identified which was homologous to alcohol dehydrogenases. The structural gene vdh of vanillin dehydrogenase was identified in a 3.8 kbp HindIII/EcoRI subfragment. Upstream of this gene an ORF was localised which was homologous to enoyl-CoA hydratases produced by various organisms.

The complementing capacity of plasmid pE5-1 was attributed to the joint obtainment of the 1.2 and 1.8 kbp EcoRI fragments (E12 and E18). Fragment E 12 was completely, and fragment E 18 partially, sequenced. The structural gene cadh of coniferyl alcohol dehydrogenase, which contained an EcoRI cleavage site, was localised in these fragments. Using chromatographic methods the enzyme was isolated from the soluble fraction of the crude extract of cells of Pseudomonas sp. HR 199 grown on eugenol. An oligonucleotide sequence was deduced from the specific N-terminal amino acid sequence. A corresponding DNA probe hybridised with fragment E12, in which the region of the cadh gene encoding the N-terminus was localised.

A eugenol- and ferulic acid-negative mutant (mutant 6167) was complemented by obtaining a 9.4 kbp EcoRI fragment (E 94) of the hybrid cosmid pE5-1. A physical map of this fragment was prepared. The complementing property was localised in a 1.9 kbp EcoRI/HindIII subfragment. This fragment had incomplete ORF's (they extended beyond the EcoRI and HindIII cleavage sites) which were homologous to acetyl-CoA acetyl transferases of various organisms and to the "medium-chain acyl-CoA synthetase" produced by Pseudomonas oleovorans. Fragment E 94 was completely sequenced. Downstream of the aforementioned ORF's an ORF was located which was homologous to β-ketothiolases. The structural gene of coniferylaldehyde dehydrogenase (caldh) was localised in a central position of fragment E 94. Using chromatographic methods the enzyme was isolated from the soluble fraction of the crude extract of cells of Pseudomonas sp. HR 199 grown on eugenol.

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The conjugative transfer of hybrid cosmid pE207 into a large number of <u>Pseudomonas</u> strains resulted in the heterologous expression of the <u>van A</u>, <u>van B</u> and <u>vdh</u> genes and the eugenol-hydroxylase genes in the transconjugants obtained. The obtainment of the plasmid of one strain allowed it to grow using eugenol as its carbon and energy source.

Materials and methods

Growth conditions of the bacteria. Strains of Escherichia coli were grown at 37°C in a Luria-Bertani (LB) or M9 mineral medium (Sambrook, J.E.F. Fritsch and T. Maniatis. 1989. Molecular cloning: a laboratory manual. 2nd Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York). Strains of Pseudomonas sp. and Alcaligenes eutrophus were grown at 30°C in a nutrient broth (NB, 0.8 % by weight) or in a mineral medium (MM) (Schlegel, H. G. et al. 1961. Arch. Mikrobiol. 38: 209-222). Ferulic acid, vanillin, vanillic acid and protocatechuic acid were dissolved in dimethyl sulphoxide and added to the respective medium in a final concentration of 0.1 % by weight. Eugenol was added to the medium directly in a final concentration of 0.1 vol.-%, or applied on filter paper (circular filters 595, Schleicher & Schuell, Dassel, Germany) to the lids of MM agar plates. For the growth of transconjugants of Pseudomonas sp., tetracyline and kanamycin were used in final concentrations of 25 μg/ml and 300 μg/ml, respectively.

Nitrosoguanidine mutagenesis. The nitrosoguanidine mutagenesis of Pseudomonas sp. HR 199 was carried out using a modified method according to Miller (Miller, J. H. 1972. Experiments in molecular genetics. Cold Spring Harbor Laboratory, Cold Spring Harbor, New York). Instead of the citrate buffer, a potassium phosphate (PP) buffer (100 mM, pH 7.0) was used. The final concentration of N-methyl-N'-nitro-N-nitrosoguanidine was 200 µg/ml. The mutants obtained were screened with regard to the loss of their capacity to utilise eugenol, ferulic acid, vanillin and vanillic acid as growth substrates.

Qualitative and quantitative detection of metabolic intermediates in culture supernatants. Culture supernatants were analysed by high-pressure liquid chromatography (Knauer HPLC) either directly or after dilution with twice-distilled water. Chromatography was carried out on Nucleosil-100 C18 (7 μ m, 250 x 4 mm). The solvent used was 0.1 vol.-% formic acid and acetonitrile.

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Purification of coniferyl alcohol dehydrogenase and coniferylaldehyde dehydrogenase. The purification processes were carried out at 4°C.

Crude extract. Cells of <u>Pseudomonas</u> sp. HR 199 grown on eugenol were washed in a 10 mM sodium phosphate buffer with a pH of 7.5, resuspended in the same buffer and disrupted by being passed through a French press (Amicon, Silver Spring, Maryland, USA) twice at a pressure of 1,000 psi. The cell homogenate was subjected to ultracentrifugation (1 h, 100,000 x g, 4°C), the soluble fraction of the crude extract being obtained as the supernatant.

Anion exchange chromatography on DEAE Sephacel. The soluble fraction of the crude extract was dialysed overnight against a 10 mM sodium phosphate buffer with a pH of 7.5 containing 100 mM NaCl. The dialysate was applied to a DEAE Sephacel column (2.6 cm x 35 cm, bed volumn [BV]: 186 ml) equilibrated with a 10 mM sodium phosphate buffer of a pH of 7.5 containing 100 mM NaCl at a flow rate of 0.8 ml/min. The column was washed with two bed volumes of a 10 mM sodium phosphate buffer with a pH of 7.5 containing 100 mM NaCl. The elution of coniferyl alcohol dehydrogenase (CADH) and coniferylaldehyde dehydrogenase (CALDH) was carried out with a linear salt gradient of 100 to 500 mM NaCl in a 10 mM sodium phosphate buffer with a pH of 7.5 (2 x 150 ml). 5 ml fractions were collected. Fractions with high CADH and CALDH activities were combined in the corresponding DEAE pools respectively.

Gel filtration chromatography on Sephadex G200. The CADH DEAE pool was concentrated in a 50 ml Amicon ultrafiltration chamber via a Diaflo ultrafiltration membrane PM 30 (both from AMICON CORP., Lexington, USA) at a pressure of 290 kPa to a volume corresponding to approx. 2% of the Sephadex G200-BV. The concentrated protein solution was applied to a Sephadex G200 column (BV: 138 ml) equilibrated with a 10 mM sodium phosphate buffer with a pH of 7.5 containing 100 mM NaCl and eluted with the same buffer at a flow rate of 0.2 ml/min. 2 ml fractions were collected. Fractions with a high CADH activity were combined in the Sephadex G200 pool.

Hydrophobic interaction chromatography on butyl Sepharose 4B. The CADH Sephadex G200 pool was adjusted to 3 M NaCl and then applied to a butyl Sepharose 4B column (BV: 48 ml) equilibrated with a 10 mM sodium phosphate buffer with a pH of 7.5 containing 3 M NaCl (flow rate: 0.5 ml/min). The

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column was then washed with 2 BV of a 10 mM sodium phosphate buffer with a pH of 7.5 containing 3 M NaCl (flow rate: 1.0 ml/min). CADH was eluted with a linearly decreasing NaCl gradient of 3 to 0 M NaCl in a 10 mM sodium phosphate buffer with a pH of 7.5 (2 x 50 ml). 4 ml fractions were collected. Fractions with a high CADH activity were combined in the HIC pool and concentrated as described above.

Chromatography on hydroxyapatite. The CALDH DEAE pool was concentrated to 10 ml in a 50 ml Amicon ultrafiltration chamber via a Diaflo ultrafiltration membrane PM 30 (both from AMICON CORP., Lexington, USA) at a pressure of 290 kPa. The concentrated protein solution was applied to a hydroxyapatite column (BV: 80 ml) equilibrated with a buffer (10 mM NaCL in a 10 mM sodium phosphate buffer with a pH of 7.0) (flow rate: 2 ml/min). The column was then washed with 2.5 bed volumes of a buffer (flow rate: 2 ml/min). CALDH was eluted with a linearly increasing sodium phosphate gradient of 10 to 400 mM NaP (in each case containing 10 mM NaCL) (2 x 100 ml). 10 ml fractions were collected. Fractions with high CALDH activity were combined in the CALDH HA pool.

Gel filtration chromatography on Superdex HR 200 10/30. The CALDH HA pool was concentrated to 200 μ l (Amicon ultrafiltration chamber, ultrafiltration membrane PM 30) and applied to a Superdex HR 200 10/30 column (BV: 23.6 ml) equilibrated with a 10 mM sodium phosphate buffer with a pH of 7.0. CALDH was eluted with the same buffer at a flow rate of 0.5 ml/min. 250 μ l fractions were collected. Fractions with high CALDH activity were combined in the CALDH Superdex pool.

Determination of coniferyl alcohol dehydrogenase activity. The CADH activity was determined at 30°C by means of an optical enzymatic test according to Jaeger et al. (Jaeger, E., L. Eggeling and H. Sahm. 1982. Current Microbiology. 6: 333-336) with the aid of a ZEISS PM 4 spectrophotometer fitted with a TE converter (both from ZEISS, Oberkochen, Germany) and a recorder. The reaction mixture with a volume of 1 ml contained 0.2 mmol of Tris/HCl (pH 9.0), 0.4 μ mol of coniferyl alcohol, 2 μ mol of NAD, 0.1 mmol of semicarbazide and a solution of the enzyme ("Tris" = tris(hydroxymethyl)-aminomethane). The reduction of NAD was monitored at l = 340 nm (e = 6,3 cm²/ μ mol). The enzyme activity was recorded in units (U), 1 U corresponding to that quantity of enzyme

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which metabolises 1 μmol of substrate per minute. The protein concentrations in the samples were determined according to the method described by Lowry et al. (Lowry, O.H., N.J. Rosebrough, A.L. Farr and R. J. Randall. 1951. J. Biol. Chem. 193: 265-275).

Determination of the coniferylaldehyde dehydrogenase activity. The CALDH activity was determined at 30°C by an optical enzymatic test with the aid of a ZEISS PM 4 spectrophotometer fitted with a TE converter (both from ZEISS, Oberkochen, Germany) and a recorder. The reaction mixture of a volume of 1 ml contained a 10 mM Tris/HCl buffer (pH 8.8), 5.6 mM coniferylaldehyde, 3 mM NAD and a solution of the enzyme. The oxidation of coniferylaldehyde to form ferulic acid was monitored at 1 = 400 nm (e = 34 cm²/ μ mol). The enzyme activity was recorded in units (U), 1 U corresponding to that quantity of enzyme which metabolises 1 μ mol of substrate per minute. The protein concentration in the samples was determined according to the method described by Lowry et al. (Lowry, O.H., N.J. Rosebrough, A.L. Farr and R. J. Randall. 1951. J. Biol. Chem. 193: 265-275).

Electrophoretic methods. The separation of protein-containing extracts was carried out in 7.4% by weight polyacrylamide gels under native conditions according to the method described by Stegemann et al. (Stegemann et al. 1973. Z. Naturforsch. 28c: 722-732) and under denaturing conditions in 11.5 % by weight polyacrylamide gels according to the method described by Laemmli (Laemmli, U.K. 1970. Nature (London) 227: 680-685). Serva Blue R was used for non-specific protein staining. For specifically staining coniferyl alcohol, coniferylaldehyde and vanillin dehydrogenase the gels were placed for 20 mins in a new 100 mM PP buffer (pH 7.0) and then incubated at 30°C in the same buffer, to which 0.08 % by weight of NAD, 0.04 % by weight of p-nitroblue-tetrazolium chloride, 0.003 % by weight of phenazine methosulphate and 1 mM of the respective substrate had been added, until the corresponding coloured bands appeared.

The transfer of proteins from polyacrylamide gels to PVDF membranes. Proteins were transferred from SDS polyacrylamide gels to PVDF membranes (Waters-Milipore, Bedford, Mass., USA) with the aid of a semidry fast blot device (B32/33 from Biometra, Göttingen, Germany) according to the manufacturer's instructions.

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Determination of N-terminal amino acid sequences. The determination of N-terminal amino acid sequences was carried out with the aid of a protein peptide sequencer (of type 477 A, Applied Biosystems, Foster City, USA) and a PTH analyser, according to the manufacturer's instructions.

Isolation and manipulation of DNA. The isolation of genomic DNA was carried out by the method described by Marmur (Marmur, J. 1961. Mol. Biol. 3: 208-218). Megaplasmid DNA was isolated according to the method described by Nies et al. (Nies, D., et al. 1987. J. Bacteriol. 169: 4865-4848). The isolation and analysis of other plasmid DNA or DNA restriction fragments, the packaging of hybrid cosmids in 1-phage particles and the transduction of E. coli. was carried out by standard methods (Sambrook, J.E.F. Fritsch and T. Maniatis. 1989. Molecular cloning: a laboratory manual. 2nd Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York).

Transfer of DNA. The preparation and transformation of competent Escherichia coli cells was carried out by the method described by Hanahan (Hanahan, D. 1983. J. Mol. Biol. 166: 557-580). Conjugative plasmid transfer between plasmid-containing Escherichia coli S17-1 strains (donor) and Pseudomonas sp. strains (recipient) and Alcaligenes eutrophus (recipient) was carried out on NB agar plates according to the method described by Friedrich et al. (Friedrich, B. et al. 1981. J. Bacteriol. 147: 198-205) or by a "minicomplementation method" on MM agar plates using 0.5 % by weight of gluconate as the carbon source and 25 μg/ml of tetracylin or 300 μg/ml of kanamycin. In this process cells of the recipient were applied in one direction in the form of an inoculation line. After 5 minutes cells of the donor strains were then applied in the form of inoculation lines crossing the recipient inoculation line. After incubation for 48 h at 30°C the transconjugants grew directly downstream of the crossing point, whereas neither the donor nor the recipient strain was capable of growth.

Hybridisation experiments. DNA restriction fragments were electrophoretically separated in an 0.8 % by weight agarose gel in a 50 mM Tris, 50 mM boric acid and 1.25 mM EDTA buffer (pH 8.5) (Sambrook, J.E.F. Fritsch and T. Maniatis. 1989. Molecular cloning: a laboratory manual. 2nd Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York). The transfer of the denatured DNA from the gel to a positively charged nylon membrane (pore size: 0.45 μm, Pall Filtrationstechnik, Dreieich, Germany), the subsequent hybridisation with

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biotinylated or ³²P-labelled DNA probes and the production of these DNA probes was carried out according to standard methods (Sambrook, J.E.F. Fritsch and T. Maniatis. 1989. Molecular cloning: a laboratory manual. 2nd Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York).

The synthesis of oligonucleotides. Using desoxynucleoside phosphoramidites as the starting material, oligonucleotides were synthesised on a 0.2 µmol scale (Beaucage, S. L., and M. H. Caruthers. 1981. Tetrahedron Lett. 22: 1859-1862). The synthesis was carried out in a Gene Assembler Plus according to the manufacturer's instructions (Pharmacia-LKB, Uppsala, Sweden). The elimination of the protecting groups was carried out by incubation for 15 h at 55°C in a 25 vol.-% aqueous ammonia solution. The oligonucleotides were finally purified in an NAP-5 column (Pharmacia-LKB, Uppsala, Sweden).

DNA sequencing. The determination of nucleotide sequences was carried out by the didesoxy chain termination method described by Sanger et al. (Sanger et al. 1977. Proc. Natl. Acad. Sci. USA 74: 5463-5467) using $[\alpha^{-35}S]dATP$ and a T7 polymerase sequencing kit (Pharmacia-LKB). 7-Deazaguanosine-5'-triphosphate, was used instead of dGTP (Mizusawa, S. et al.

Deazaguanosine-5'-triphosphate was used instead of dGTP (Mizusawa, S. et al. 1986. Nucleic Acids Res.14: 1319-1324). The products of the sequencing reactions were separated in a 6% by weight polyacrylamide gel in a 100 mM Tris/HCl, 83 mM boric acid and 1 mM EDTA buffer (pH 8.3) containing 42 % by weight urea, an S2 sequencing apparatus (GIBCO/BRL, Bethesda Research Laboratories GmbH, Eggenstein, Germany) being used according to the manufacturer's instructions. After electrophoresis the gels were incubated for 30 mins in 10 vol.-% acetic acid and, after washing briefly in water, dried for 2 hours at 80°C. Kodak X-OMAT AR X-ray films (Eastman Kodak Company, Rochester, NY, USA) were used for the autoradiography of the dried gels. In addition DNA sequences were also determined "non-radioactively" with the aid of an "LI-COR DNA Sequencer Model 4000L" (LI-COR Inc., Biotechnology Division, Lincoln, NE, USA) using a "Thermo Sequenase fluorescent labelled primer cycle sequencing kit with 7-deaza-dGTP" (Amersham Life Science, Amersham International plc, Little Chalfont, Buckinghamshire, England), in each case according to the manufacturer's instructions.

Various sequencing strategies were used: With the aid of synthetic oligonucleotides sequencing was carried out by the "Primer-hopping Strategy" described by

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Strauss et al. (Strauss, E. C. et al. 1986. Anal. Biochem. 154: 353-360). If only "universal" and "reverse primers" were used hybrid plasmids were used as "template DNA", the inserted DNA fragments of which had been unidirectionally shortened with the aid of an "Exo III/Mung Bean Nuclease Deletion" kit (Stratagene Cloning Systems, La Jolla, Cal., USA) according to the manufacturer's instructions.

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Chemicals, biochemicals and enzymes: Restriction enzymes, T4 DNA ligase, lambda DNA and enzymes and substrates for the optical enzymatic tests were obtained from C. F. Boehringer & Söhne (Mannheim, Germany) or from GIBCO/BRL (Eggenstein, Germany). [a-35S]dATP and [g-32P]ATP were obtained from Amersham/Buchler (Braunschweig, Germany). NA-type agarose was obtained from Pharmacia-LKB (Uppsala, Sweden). All the other chemicals were from Haarmann & Reimer (Holzminden, Germany), E. Merck AG (Darmstadt, Germany), Fluka Chemic (Buchs, Switzerland), Serva Feinbiochemica (Heidelberg, Germany) or Sigma Chemie (Deisenhofen, Germany).

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Examples

Example 1

The isolation of mutants of the <u>Pseudomonas</u> sp. HR 199 strain with defects in the catabolism of eugenol

The <u>Pseudomonas</u> sp. HR 199 strain was subjected to nitrosoguanidine mutagenesis in order to isolate mutants with defects in the catabolism of eugenol. The mutants obtained were classified according to their capacity to utilise eugenol, ferulic acid and vanillin as their carbon and energy source. Mutants 6164 and 6165 were no longer capable of utilising eugenol as a carbon and energy source, although, as in the case of the wild type, they were capable of utilising eugenol and vanillin. Mutants 6167 and 6202 were no longer capable of utilising eugenol and ferulic acid as their carbon and energy source, although, as in the case of the wild type, they were capable of utilising vanillin. The abovementioned mutants were used in the subsequent molecular-biological analyses.

15 Example 2

Construction of a <u>Pseudomonas</u> sp. HR 199 gene library in the cosmid vector pVK100

The genomic DNA of the <u>Pseudomonas</u> sp. HR 199 strain was isolated and subjected to partial restriction digestion with <u>Eco</u>RI. The DNA preparation thus obtained was ligated with vector pVK100 cut by <u>Eco</u>RI. The DNA concentrations were relatively high in order to accelerate the formation of concatemeric ligation products. The ligation materials were packaged in l-phage particles which were subsequently used for transduction of <u>E. coli</u> S17-1. The selection of the transductants was carried out on tetracycline-containing LB agar plates. In this manner 1330 transductants were obtained which contained various hybrid cosmids.

Example 3

The identification of hybrid cosmids containing essential genes of eugenol catabolism

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The hybrid cosmids of the 1330 transductants were transferred conjugatively to mutants 6164 and 6165 by a minicomplementation process. transconjugants were examined on MM plates containing eugenol for their capacity to grow again on eugenol (complementation of the respective mutant). Mutant 6164 was complemented by the obtainment of hybrid cosmid pE5-1, which contained a 1.2 kbp, a 1.8 kbp, a 3 kbp, a 5.8 kbp and a 9.4 kbp EcoRI fragment The E. coli S17-1 strain containing this hybrid cosmid was in cloned form. deposited at the "Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH" (DSM) under the number DSM 10440. Mutant 6165 was complemented by the obtainment of the hybrid cosmids pE207 or pE115 respectively. complementing capacity was attributed to a 23 kbp EcoRI fragment which was contained in cloned form in the hybrid cosmid pE207 as the only EcoRI fragment, whereas hybrid cosmid pE115 additionally contained a 3 kbp and a 6 kbp EcoRI fragment. The E. coli S17-1 strain containing hybrid cosmid pE207 was deposited at the DSM under the number DSM 10439.

Example 4

The analysis of the 23 kbp EcoRI fragment (E230) of the hybrid cosmid pE207

Fragment E230 was isolated preparatively from <u>EcoRI</u>-digested hybrid cosmid pE207 and ligated to pBluescript SK⁻-DNA digested with <u>EcoRI</u>. Using the ligation material <u>E</u>. <u>coli</u> XL1-Blue was transformed. Following "blue-white" selection on LB-Tc-Amp agar plates containing X-Gal and IPTG, "white" transformants were obtained whose hybrid plasmids pSKE230 contained the fragment E230 in cloned form. With the aid of this plasmid and by using various restriction enzymes a physical map of the fragment E230 was prepared (Fig. 1).

By cloning subfragments of E230 in vectors pVK101 and pMP92, both of which have a broad host specturm and are also stable in pseudomonads, followed by conjugative transfer into mutant 6165, the region complementing mutant 6165 was localised in a 1.8 kbp KpnI fragment (K18). After cloning this fragment in pBluescript SK⁻ the nucleotide sequence was determined, the gene of the cytochrome C subunit of eugenol hydroxylase being identified. The gene product of 117 amino acids had an N-terminal leader peptide (MMNVNYKAVGAS-LLLAFISQGAWA) and 32.9% identity (via a region of 82 amino acids) with the

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cytochrome C subunit of p-cresol methylhydroxylase produced by <u>Pseudomonas</u> <u>putida</u> (McIntire et al. 1986. Biochemistry 25:5975-5981).

By cloning the <u>Kpn</u>I subfragments of E230 adjacent to K18 in pBluescript SK-and sequencing, additional open reading frames (ORF) were identified, one of which codes for the flavoprotein subunit of eugenol hydroxylase and was highly homologous to the flavoprotein subunit of p-cresol methylhydroxylase produced by <u>Pseudomonas putida</u>. An additional ORF was found to be highly homologous to g-glutamyl cysteine synthetase (the first enzyme in the biosynthesis of glutathione) produced by <u>Escherichia coli</u> (Watanabe et al. 1986. Nucleic Acids Res. 14: 4393-4400).

In the soluble fraction of the crude extract of <u>E</u>. <u>coli</u> (pSKE230) vanillin dehydrogenase was detected by specific activity staining in a polyacrylamide gel. By subcloning in pBluescript SK⁻ and analysis of soluble fractions of the crude extracts of the transformants obtained, the vanillin dehydrogenase gene (<u>vdh</u>) was localised in a 3.8 kbp <u>HindIII/Eco</u>RI subfragment of E230. The complete nucleotide sequence of this fragment was determined. The molecular weight of the vanillin dehydrogenase was 50,779, as confirmed by SDS polyacrylamide gel electrophoresis. The amino acid sequence was highly homologous to other aldehyde dehydrogenases of various origins.

Upstream of the <u>vdh</u> gene an additional ORF was identified which was homologous to enoyl-CoA hydratases. The calculated molecular weight of 27,297 was confirmed by SDS polyacrylamide gel electrophoresis.

By sequencing the 5.0 kbp <u>HindIII</u> subfragment of E230, which had also been cloned in pBluescript SK⁻, an ORF was identified which was highly homologous to the lignostilbene-a,b-dioxygenase produced by <u>Pseudomonas paucimobilis</u>. By complete sequencing of the fragment E230 two additional ORF's were identified which were homologous to formaldehyde-dehydrogenases (fdh) and alcohol dehydrogenases (adh) (cf. Fig. 1).

Example 5

The analysis of the region of hybrid cosmid pE5-1 complementing mutant 6164

Mutant 6164 was complemented by the obtainment of hybrid cosmid pE5-1 which contained a 1.2 kbp (E12), a 1.8 kbp (E18), a 3 kbp (E30), a 5.8 kbp (E58) and a 9.4 kbp (E94) EcoRI fragment in cloned form (Fig. 1). By digesting pE5-1 with EcoRI and subsequent religation a derivative (pE106) of this hybrid cosmid was obtained which only contained fragments E12, E18 and E30. Following conjugative transfer into mutant 6164 this plasmid was however capable of complementing the latter, as a result of which corresponding transconjugants were once again capable of growing on eugenol as a carbon and energy source.

After digesting plasmid pE106 with <u>Eco</u>RI, gel-electrophoretic separation of the digestion material in a 0.8 % by weight agarose gel and transfer of the DNA to a nylon membrane, hybridisation was carried out with a ³²P-labelled oligonucleotide probe of the following sequence:

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ATG	CAA	CTC	ACC	AAC	AAA	AAA	ATC	GT-3'
	G	G	C	T	G	G	T	
	G	G	C		G	G		
	G	T	G		G	G		
			G		G	G		
			T		G	G		

The sequence of this gene probe had been deduced from the N-terminal amino acid sequence of coniferyl alcohol dehydrogenase (CADH) (see below) purified from Pseudomonas sp. HR 199. With the aid of this probe the region of the cadh gene encoding the N-terminus of the CADH was localised in fragment E12. This fragment and parts of the adjacent fragment E 18 were also sequenced and the complete sequence of the cadh gene thus determined. The amino acid sequence deduced from cadh was homologous to other alcohol dehydrogenases of class I, group II (according to Matthew and Fewson. 1994. Critical Rev. Microbiol. 20(1): 13-56).

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Purification and characterisation of coniferyl alcohol dehydrogenase

Pseudomonas sp. HR 199 was grown on eugenol. The cells were harvested, washed and disrupted with the aid of a French press. The soluble fraction of the crude extract obtained after ultracentrifugation had a specific activity of 0.24 U/mg of protein. By means of chromatography on DEAE Sephacel an 11.7-fold enrichment of CADH was obtained in a yield of 83.7 %. By means of chromatography on Sephadex G200 a 6.8-fold enrichment of CADH was obtained in a yield of 11.2 %. By means of chromatography on butyl Sepharose 4B a 70.6-fold enrichment of CADH was obtained in a yield of 7.8 %.

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With the aid of this method a preparation was obtained which displayed a band at 27 kDa according to SDS polyacrylamide gel electrophoresis. The purification factor was 64 and the yield 0.8 %.

Optimum temperature and thermal stability

The optimum temperature for the reaction catalysed with CADH was 42°C. The enzyme was however sensitive to heat. The half-lives were as follows: $T_{1/2}$ (34°C) = 5 mins, $T_{1/2}$ (39°C) = 1 min, $T_{1/2}$ (42°C) <1 min.

Optimum pH

The optimum pH for the reaction catalysed by CADH was 10.9 in a 25 mM MOPS buffer. At higher pH values a decrease in activity due to denaturation was observed.

Apparent molecular weight

The molecular weight of native CADH was determined with the aid of FPLC by gel filtration on Superdex 200HR 10/30 at 54.9 kDa, which suggests a a₂ subunit structure.

N-terminal amino acid sequence

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The determination of the N-terminal amino acid sequence of the purified protein revealed the following result:

(Sequence in the single letter code; ?: definition not possible; (): not certain; in the second row an amino acid is mentioned which may also apply)

Example 7

Purification and characterisation of coniferylaldehyde dehydrogenase

Pseudomonas sp. HR 199 was grown on eugenol. The cells were harvested, washed and disrupted with the aid of a French press. The soluble fraction of the crude extract obtained after ultracentrifugation displayed a specific activity of 0.43 U/mg protein. By chromatography on DEAE Sephacel a 6.6-fold enrichment of CALDH was obtained in a yield of 65.3 %. By chromatography on hydroxyapatite a 63-fold enrichment of CALDH was obtained in a yield of 33 %. By chromatography on Superdex HR 200 an 81-fold enrichment of CALDH was obtained in a yield of 13 %. With the aid of this method a preparation was obtained which, according to SDS polyacryamide gel electrophoresis, displayed a band at approx. 49 kDa.

20 Optimum temperature and thermal stability

The optimum temperature of the reaction catalysed by CALDH was 26°C. The enzyme was sensitive to heat. The half-lives were as follows: $T_{1/2}$ (31°C) = 5 mins, $T_{1/2}$ (34°C) = 2.5 mins, $T_{1/2}$ (38°C) = 1 min.

Optimum pH

The optimum pH for the reaction catalysed by CALDH was 8.8 in a 100 mM Tris/HCl buffer. At this pH value the enzyme is however already unstable (87 % decrease in activity within 5 mins). At lower pH values the enzyme is more stable (e.g. pH 6.0: 50 % decrease in activity within 4 hours).

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Substrate specificity

The enzyme not only accepts coniferylaldehyde (100 %) but also transcinnamaldehyde (96.7 %), sinapyl aldehyde (76.7 %), p-anisaldehyde (23.1 %), benzaldehyde (17.8 %), 3,5-dimethoxy-benzaldehyde (7.6 %) and 3-hydroxy-benzaldehyde (1.7 %) as substrates.

The $\rm K_M$ value of CALDH for coniferylaldehyde is in the range between 0.007 and 0.012 mM at a $\rm V_{max}$ of approx. 9 to 15 U/ml. The $\rm K_M$ value of CALDH for NAD is 0.334 mM at a $\rm V_{max}$ of 14.2 U/ml. Compared with NAD, NADP is accepted at a rate of 4.3 %.

10 N-terminal amino acid sequence

The determination of the N-terminal amino acid sequence of the purified protein revealed the following result:

1 SILGLNGAPVGAEQLGSAL(D) 20

(sequence in the one-letter code; (): not certain).

15 Example 8

Localisation and sequencing of the coniferylaldehyde dehydrogenase gene (caldh)

The N-terminal amino acid sequence was definitively assigned to an amino acid sequence deduced from the DNA sequence of fragment E94 of plasmid pE5-1. Thus the CALDH structural gene <u>caldh</u> is localised in E94. The amino acid sequence deduced from <u>caldh</u> was homologous to other aldehyde dehydrogenases.

Example 9

The complementation of other mutants displaying defects in the catabolism of eugenol using hybrid cosmids pE207 and pE5-1

Following NMG mutagenesis, mutants 6167 and 6202 had been obtained which were no longer capable of utilising eugenol and ferulic acid as their carbon and energy source (see above). The obtainment of plasmid pE207 meant that, after

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conjugative transfer, mutant 6202 was once again capable of utilising the aforementioned substrates. This mutant is complemented by the gene homologous to enoyl-CoA hydratase.

The obtainment of plasmid pE5-1 meant that, after conjugative transfer, mutant 6167 was once again capable of utilising the abovementioned substrates. By individually cloning the EcoRI fragments of pE5-1 in pHP 1014 and the conjugative transfer of these plasmids into mutant 6167 the complementing property was localised in fragment E94. A physical map of fragment E94 was prepared after cloning in pBluescript SK⁻ and digestion with various restriction enzymes. By cloning subfragments of E94 in the vectors pVK101 and pMP92, followed by conjugative transfer into mutant 6167, the region complementing mutant 6167 was localised in a 1.9 kbp EcoRI/HindIII fragment (EH19). After cloning this fragment in pBluescript SK⁻ and sequencing, 2 ORF's were identified which were homologous to acetyl-CoA acetyltransferases and to "medium-chain acyl-CoA synthetase" produced by Pseudomonas oleovorans. By completely sequencing fragment E94, additional ORF's were identified which were homologous to regulator proteins and a chemotaxis protein (cf. Fig. 1).

Example 10

Determination of the chromosomal coding of the genes for the catabolism of eugenol in <u>Pseudomonas</u> sp. HR 199

Since <u>Pseudomonas</u> sp. HR 199 has a megaplasmid of a size of approx. 350 kbp, a hybridisation experiment was carried out to examine whether the genes for the catabolism of eugenol were localised in this megaplasmid or in the chromosome. For this purpose megaplasmid preparations of the wild type and of the mutants were separated in an 0.8 % by weight agarose gel. The chromosomal and megaplasmid DNA was blotted onto a nylon membrane and then hybridised against a biotinylated HE38 DNA probe. A hybridisation signal was only obtained with the chromosomal DNA and not with the megaplasmid DNA. Thus the genes for the catabolism of eugenol in <u>Pseudomonas</u> sp. HR 199 are coded in the chromosome.

Example 11

The heterologous expression of genes for the catabolism of eugenol from <u>Pseudomonas</u> sp. HR 199 in other <u>Pseudomonas</u> strains and in <u>Alcaligenes eutrophus</u>.

The plasmid pE207 and a pVK101 hybrid plasmid containing fragment H110 (pVKH110) were conjugatively transferred to A. eutrophus and into Pseudomonas strains which were not capable of metabolising eugenol, vanillin or vanillic acid. The transconjugants obtained were not only examined for their capacity to grow on MM agar plates containing eugenol, vanillin or vanillic acid but also some transconjugants were incubated with eugenol in an MM liquid medium. By means of HPLC analysis of the culture supernatants some of the transconjugants were found to metabolise eugenol.

In this analysis the functional expression of the <u>vdh</u> gene in transconjugants of <u>P</u>. <u>stutzeri</u>, <u>P</u>. <u>asplenii</u>, <u>Pseudomonas</u> sp. DSM13, <u>Pseudomonas</u> sp. DSM15a and <u>Pseudomonas</u> sp. D1 was determined.

Transconjugants of the strain <u>Pseudomonas</u> sp. D1, which contained the plasmid pE207, were capable of growing using eugenol as their carbon and energy source. In corresponding transconjugants of <u>P. testosteroni</u> LMD3324, <u>P. fluorescens</u> TypeB, <u>P. stutzeri</u> DSM 50027, <u>Pseudomonas</u> sp. DSM 1455 and <u>P. fragi</u> DSM3456 functional expression of the eugenol hydroxylase genes was also observed which resulted in the secretion of intermediates of the catabolism of eugenol (coniferyl alcohol, coniferylaldehyde, ferulic acid, vanillin, vanillic acid) into the culture medium. Growth of these transconjugants on eugenol was however not observed.

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SEQUENCE LISTING

- (1) GENERAL INFORMATION:
 - (i) APPLICANT:
 - (A) NAME: Haarmann & Reimer GmbH
 - (B) STREET: Rumohrtalstrasse 1
 - (C) CITY: Holzminden
 - (E) COUNTRY: Deutschland
 - (F) POSTAL CODE (ZIP): 37603
 - (G) TELEPHONE: 0214-3067988
 - (H) TELEFAX: 0214-303482
 - (ii) TITLE OF INVENTION: Syntheseenzyme fuer die Herstellung von Coniferylalkohol, Coniferylaldehyd, Ferulasaeure, Vanillin und Vanillinsaeure und deren Verwendung
 - (iii) NUMBER OF SEQUENCES: 42
 - (iv) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Floppy disk
 - (B) COMPUTER: IBM PC compatible
 - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)
- (2) INFORMATION FOR SEQ ID NO: 1:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32679 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Pseudomonas sp.
 - (B) STRAIN: HR199
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 3146..3997
 - (D) OTHER INFORMATION:/gene= "ORF1"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

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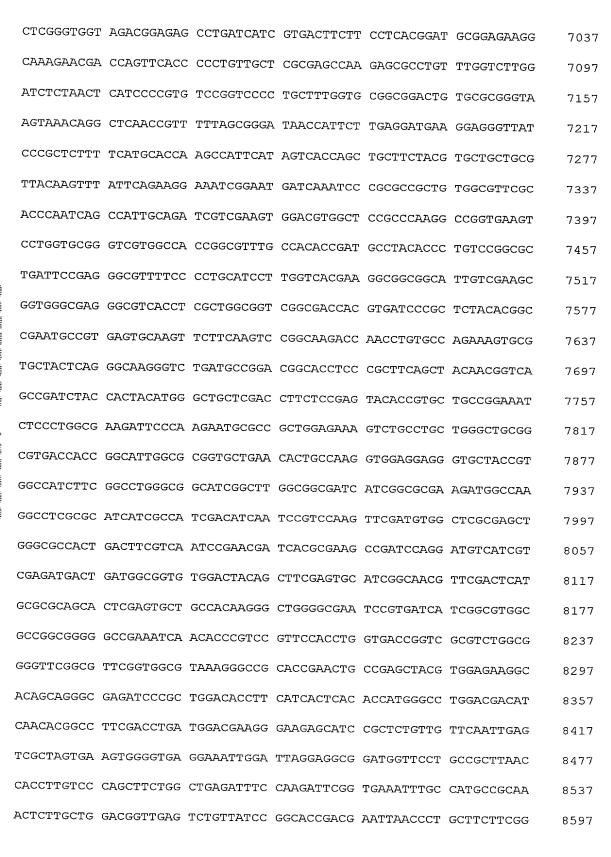
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	Ala		CAA Gln								Tyr					3460
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			CAC His													3604
			TTG Leu													3652
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			GGT Gly													3748
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			CCC Pro		Gly											3892

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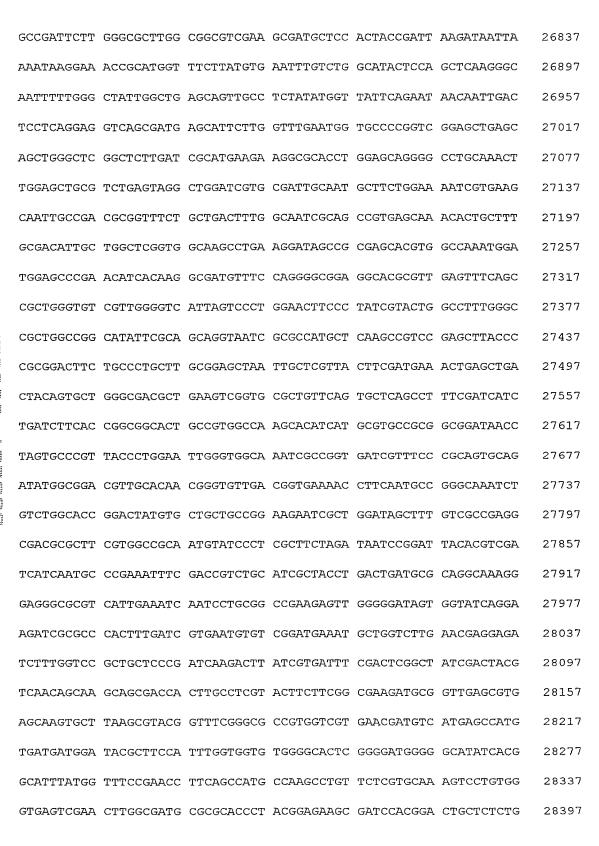
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TTAGTGGGTG	CCCTTGAGCG	AGACAGTACC	CTGCGCGAAC	GCTTCTTCGC	TCGCATGAAG	22217
CTGTTCTTCT	TCGCGGCGGC	TGGGTTGTCG	CAAGGGATCT	GGGATCGTTT	GGACCGGGTC	22277
GCTGAACAGC	ACTGTGGTGA	GCGCATTCGC	ATGATGGCGG	GTCTGGGCAT	GACGGAGACT	22337
GCTCCTTCCT	GCACTTTTAC	CACCGGACCG	CTGTCGATGG	CTGGTTACAT	TGGGCTGCCA	22397
GCGCCTGGCT	GCGAGGTCAA	GCTCGTTCCG	GTCGATGGGA	AATTGGAAGG	GCGTTTCCAT	22457
GGTCCGCACG	TCATGAGCGG	CTACTGGCGT	GCTCCTGAAC	AAAATGCCCA	AGCGTTCGAC	22517
GAGGAAGGCT	ATTACTGCTC	CGGTGATGCC	ATCAAATTGG	CAGATCCTGC	CGATCCTCAG	22577
AAAGGTCTGA	TGTTTGACGG	TCGAATTGCT	GAAGACTTCA	AGCTGTCCTC	AGGGGTATTT	22637
GTCAGCGTTG	GGCCATTGCG	CACGCGGGCG	GTTCTGGAAG	GCGGCTCTTA	CGTCCTGGAC	22697
GTAGTGGTTG	CTGCTCCTGA	TCGTGAATGC	CTTGGATTGC	TCGTGTTTCC	GCGTCTTCTC	22757
GACTGCCGTG	CCTTGTCGGG	GCTAGGAAAA	GAGGCGTCGG	ACGCCGAGGT	GCTTGCCAGT	22817
GAGCCGGTTC	GGGCCTGGTT	TGCTGACTGG	CTCAAACGAC	TCAATCGAGA	AGCAACTGGC	22877
AATGCCAGTC	GCATCATGTG	GGTAGGGCTC	CTCGATACGC	CGCCGTCGAT	TGATAAGGGC	22937
GAGGTCACTG	ACAAGGGCTC	GATCAACCAG	CGCGCTGTTT	TGCAATGGCG	GTCGGCGAAA	22997
GTTGATGCGC	TGTATCGTGG	TGAAGATCAA	TCCATGCTGC	GTGACGAGGC	CACACTGTGA	23057
GTTGGTCAGG	GGGGGCTTAC	TCGGCGTTTT	CCGACACTGC	GTTGGTTGCG	GCAGTGCGCA	23117
CCCCCTGGAT	TGATTGCGGG	GGTGCCCTGT	CGCTGGTGTC	GCCTATCGAC	TTAGGGGTAA	23177
AGGTCGCTCG	CGAAGTTCTG	ATGCGTGCGT	CGCTTGAACC	ACAAATGGTC	GATAGCGTAC	23237
TCGCAGGCTC	TATGGCTCAA	GCAAGCTTTG	ATGCTTACCT	GCTCCCGCGG	CACATTGGCT	23297
TGTACAGCGG	TGTTCCCAAG	TCGGTTCCGG	CCTTGGGGGT	GCAGCGCATT	TGCGGCACAG	23357
GCTTCGAACT	GCTTCGGCAG	GCCGGCGAGC	AGATTTCCCA	AGGCGCTGAT	CACGTGCTGT	23417
GTGTCGCGGC	AGAGTCCATG	TCGCGTAACC	CCATCGCGTC	GTATACACAC	CGGGGCGGGT	23477





GACTTGGCT	G ATGTCGGGG	A CAGCAGGCG(C AAGGATGAAA	A TCGGTCAGTT	GCAAAGTGCA	25157
ACTAGGCGG	A TGGCGATTG	G ACTGCGTAAT	r ctggtcggt	F ATATTGGTC	A AAGTCGTGCG	25217
CAACTGGTT	F CATCGTCCA	G CGACCTTTC	G GCCATCTGT	CTCAGGCTCA	A GATTGATGTC	25277
GAGTGCCAG	A AGCTTTCGGT	CGCCCAGGTC	C TCTACCGCCG	F TGAACGAGTI	GGTTGAAACC	25337
GTCCAGGCA	A TAGCAAAAA	G CACCGAAGAG	GCAGCAACAG	TCGCCGTCTT	GGCCGATGAA	25397
AAGGCACGC	GTGGTGAAA	F TGTCGTTAAC	C AAGGCCGTTG	ATTTCATTGA	GCACCTCTCC	25457
GGAGATATG	G CGGAACTGGG	G AGACGCAATG	GAGCGGCTTC	AGAACGACAG	TGCGCAGATC	25517
AATAAGGTAG	TAGACGTCAT	' TAAGGCTGTG	GCGGAGCAGA	CCAATCTGCT	AGCCCTGAAT	25577
GCGGCGATA	AGGCGGCCCG	TGCAGGAGAG	CAGGGCAGGG	GCTTTGCGGT	CGTGGCGGAT	25637
GAGGTTCGT	CTTTGGCGAT	GCGCACCCAA	CAATCGACCA	AAGAAATTGA	GAGGCTAGTG	25697
GTTTCATTGC	AGCAGGGAAG	TGAAGCTGCG	GGCGAGTTGA	TGCGGCGTGG	CAAGGTCCGG	25757
ACGCATGACG	TCGTTGGATT	GGCCCAGCAA	GCCGCGCGCC	GCGCTACTCG	AAATTACCCA	25817
GCTGTCGCCG	GCATCCAAGC	GATGAACTAT	CAGATCGCCG	CTGGAGCAGA	GCAGCAAGGG	25877
GCTGCTGTGG	TTCAAATCAA	CCAGAATATG	CTTGAAGTGC	ATAAGATGGC	TGACGAGTCC	25937
GCCATTAAAG	CGGGACAGAC	CATGAAGTCA	TCGAAGGAGC	TTGCTCACCT	CGGCAGTGCG	25997
CTACAAAAAT	CCGTTGATCG	ATTCCAGCTG	TAGCGCTCCG	GGTGGCTGAA	ACGCGCATTT	26057
TCGTTAAGGT	CTTCAGCGCG	GTCTGCTGGT	GCGTGGGCCG	CTAGCCTAAC	TGTTGCGCTT	26117
CAGGCTCCGC	ATGGATCTTG	TGCAGCAGCA	ATAGCAATTG	TTCACGTTCG	TCATCACTCA	26177
GCATCGACGT	CGCGTCTTGG	TCGCTCTGTA	CCACGATCTT	CTTCAGCTCT	TTGAGCTGCG	26237
TCTCCCCAGC	TTTGCTGAGA	AATATCCCAT	AGGAACGCTT	GTCCGGCTTG	CAGCGCACGC	26297
GCACAGCAAG	GCCGAGCTTC	TCGAGCTTGT	TCAGCAAGGG	AACCAGTTGT	GGTGGTTCGA	26357
TTGCGAGCAT	CCGCGCTAGG	TCAGCCTGCA	TAAGCCCAGG	GCTCGCTTCG	ATGATTAGAA	26417
GTGCCGACAG	CTGCGCCGGG	CGTAGGTCAT	ATGGCGTCAG	GGCTTCAATC	AGGCCCTGAG	26477
CGAGCTTCAG	CTGTGAGCCG	GCGTAAGGCA	TAGCCAATCA	ATTGATTCAG	GAGCGTATCG	26537
CCCGGTTCTA	TCAGCGGGCC	GCTTTCGAAA	GTCATGGTGT	TAGCCGGTAG	GGTCTTTTTC	26597
TTGGCCATGC	TTGTTGCCTG	AACCTTCGTT	GACATAGGGC	AGAGGTGCGT	TTGCCGCTTC	26657
GCTTCGCGAT	GAACCGCATC	GAGATGCTGA	GGTCAGGATT	TTTCCTTAAC	TCGCGTAAGC	26717
ATTCTGTCAT	TTTTTTGGTG	GCTTTGAACA	GCCTGATGAA	AGGTGGTCTC	GCCCTTTGAG	26777



TCCTCCTTTC	AACGGAGTGT	TAGAACCGTT	GGTAGTGGTT	TTGGACGGGC	CCAGGAGCAT	28457
GCGCTTCTGG	GCCCGTTTCT	TGAGTATTCA	TTGGATAGTC	ACGCGTGGTA	GCTTCGAGCC	28517
TGCACAGCTG	ATGAGCACCC	TGGAAGGCGC	GCTGTACGCG	GACGACTGGG	TTCATCTTCG	28577
CCATTCATGA	CGGAACTCCG	TTCCCCAGTA	CCGCGATGAC	TATTTTGCCT	CTTCCGATGT	28637
CCGATTCCAC	GCCGCCTGAC	GCTAAGCGGG	GGCGGGGGCG	CCCGCATCCC	AGCCCAGACA	28697
GCAACAAATG	AGTAGGCTCT	TGGATGCCGC	GGCGGCTGAG	ATTGGTAACG	GCAATTTCGT	28757
CAATGTGACG	ATGGATTCGA	TTGCCCGTGC	TGCCGGCGTC	TCAAAAAAA	CGCTGTACGT	28817
CTTGGTGGCG	AGCAAGGAAG	AACTCATTTC	CCGGTTAGTG	GCTCGAGACA	TGTCCAACCT	28877
TGAGCTGCTG	CTTTGTCACG	AGGTTGAGTC	TGCGGAGGCC	CTTCAGGATG	AGTTGCGAAA	28937
CTATCTGCTG	CTCTGGGCGC	GCTTGACCTT	GTCCCCTCTT	GCTTTGGGCA	TTTTTCTGAT	28997
GGCCGTGCAG	GGGCGTGAAA	GTGCCCGGG	CCTGGCGAGA	ATCTGGTATC	GAGAGGGGGC	29057
AGAGCGTTGC	CTCAGCTTGC	TTCGGGGATG	GTTGGCAAGG	ATGGCAAGCC	GGGAGCTGAT	29117
CGCTCCTGGA	GATATCGACT	CCGCAGTGGA	GCTTATCGAT	TCGCTCCTGA	TCTCACAGCC	29177
TTTGAAATTA	TTTGGCCTGG	GGATCCAGAG	CGGCTGGACC	GATGATCAGA	TCAATCAACG	29237
GGTCACAATC	GCTCTCGATG	CATTCCGTCG	GTGCTATGTC	GTTTAGCACC	GTTCTCGCGG	29297
GCTGTGGCGG	CGTGACCTAT	TTGTCTAGTG	GTCGGCGCGA	AATTCGATAA	GAAAGCTGGG	29357
CGCGAGTGAG	GCCGAGCCGG	CGGGCAGCTT	CCGAGACATT	GCCTTTCACC	TGGCCCAGAG	29417
CATGGCTAAT	CATCGCGTCC	TCCACTTCTT	GCAGCGTCAT	CGCGCTCAGG	TCCTTTGAGT	29477
CAAGCGGCGA	GTCGATTGTG	CTGGTCGGTT	TGGAGAAGGA	AGTACTTGGG	CTGCCAGTTT	29537
CCTGTGGCTG	ATTATCTTGA	GCGGTGGCCA	GGATGCCGCT	GGCCCCAATG	GAGAACATCG	29597
GTTGAGTCAG	TCGTTCACCG	CTAGTGAAGA	GGTGGCTCAC	GTCAATGGCT	CCATCCTCCG	29657
GAGCGCTGAT	GACTCCGCGC	TCCACCAAAT	TTTGAAGCTC	CCGGATGTTT	CCTGGAAAGT	29717
CGTAGCCAAG	CAGGGCATTG	GCTGCACGTG	GAGTGAATCC	GCTGACCACC	CGGCTATGAC	29777
GCTGATTGAA	GCGGTGCAGG	AAATAGGTCA	TCAGGAGGG	AATGTCTTCC	TTCCTCTCTC	29837
GAAGCGGCGG	GAGGTGGATC	GGGTAAACAT	TGAGGCGGAA	AAAAAGGTCC	TCGCGGAACT	29897
CGCCGCGCTG	GACGCCTGCG	CGAAGATCGA	CATTGGTTGC	GGCTACCACA	CGGACGTCAA	29957
CCTTGAGTGT	CCTGCTTCCG	CCAACCCGTT	CGACCTCCGA	CTCTTGCAGG	GCGCGAAGTA	30017
ACTTCCCTTG	GGCCACGAGG	CTTAGCGTCC	CTATCTCGTC	AAGGAATAGT	GTGCCGCCCG	30077

AAGCGCGCTC	GAACCGTCCT	GCTCGAGATT	GGGTGGCGCC	GGTAAACGCC	CCCCGTTCGA	30137
CGCCGAACAA	CTCGGACTCC	ATCAGGGTTT	CGGGAATACG	TGCGCAATTG	ACCGCAACAA	30197
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CACCTGATTC	ACCCGTAAAC	AGTACCGTCG	CCTCCGTGGG	TGCTACGCGC	TTCAGCATGT	30317
GGCAGGCAGC	ATTGAATGCC	GAGGAAATTC	CCACCATGTC	GTGTTCCGAT	GCAGTGCTTG	30377
AGTCTGCGGC	GGAGTGATGG	GGAGTGTTCC	TTTGTCCCTG	CTGCGTTCTT	CGTCTCTGCG	30437
GCGTGCTTGG	TTGCCGACAA	ATGGTTGCGC	TAAGCGCCGC	CAAGTCCTCT	TCGGCGTCTT	30497
CCCATTCTTC	CGCTGGCTTG	CCGATCATGC	GGCAGATCTG	CGAACCCGTG	GAGCGGCATT	30557
CCACCTCTCG	GTAAAGGATG	AGGCGACCAA	CCAGCGCGGA	CGTATAGCCA	ATGGCATAAC	30617
CCGTCTGCGT	CCAGCACGCG	GGCTCGGTGC	CGATGCCGTA	GTGCGCAATA	TGTTCATCAT	30677
CTTCGCTCGA	ATGGTGCCAG	AGGAATTCGC	CGTAGTAGGT	CCCCAAATCC	ATGTCGAAGT	30737
CGAAGTGGAT	CGGCTCCACG	CGTACTGCGC	CTTCCAGAGA	GTGCAAGTTC	GGGCCGGCGG	30797
CAAATAGGGA	GAGCGGATCG	GCGTTGCTGA	AGCGCTCCTT	CAGAAGGGCG	GCATCTTTGG	30857
CGCCGCAGTG	GTAACCGGTT	CGCAGCATGA	TTCCGCGGGC	GCGGGCGAAG	CCCACGCTTT	30917
CAATTAATTC	GCGTCGCAAT	GCACCCAGTC	CGCTGCTGTG	GAGGAGCAGC	ATTCGCGCGC	30977
CGTTCAACCA	GATGCGTCCA	TCGCCAGGGC	TGAAAAGGAG	GGATTCAGTG	AGGTCATGAA	31037
GGGAGGGGAC	GGCGCCTGGC	TCCAATTGCT	CGATGGCGCC	GCGATTGAGT	GTCTTGGGCG	31097
CGGTCTTGGA	GAGTTCGGCT	AGGGAGATAA	ATTTGCTGGC	CATGGTGGCG	GCCCCTGATG	31157
GGTTGGATGA	TTTTCTGCAT	TCTGCATCAT	GAAATTCATG	AAATCATCAC	TTTTCGGGGG	31217
GTGGGTGCAC	GGGATTGAAG	GTTGCTAGGA	GAGTGCATTG	CTCGTAAGCC	CAGGAAGCAC	31277
GCGGGTTTCA	GGATGGTGCA	TGGAAATGGC	ATGAGCTTTG	CTGGATATGA	TTAGAGACAT	31337
TAACTATTTT	GGCGGAATGG	AAGCACGATT	CCTCGCCCGG	TAGAGCGGTA	ACCGCGACAT	31397
TCAGGACCGT	AAAAAGGAAA	GAGCATGCAA	CTGACCAACA	AGAAAATCGT	CGTCACCGGA	31457
GTGTCCTCCG	GTATCGGTGC	CGAAACTGCC	CGCGTTCTGC	GCTCTCACGG	CGCCACAGTG	31517
ATTGGCGTAG	ATCGCAACAT	GCCGAGCCTG	ACTCTGGATG	CTTTCGTTCA	GGCTGACCTG	31577
AGCCATCCTG	AAGGCATCGA	TAAGGCCATC	TCTCAGCTGC	CGGAGAAAT	TGACGGACTC	31637
TGCAATATCG	CCGGGGTGCC	CGGCACTGCC	GATCCTCAGC	TCGTCGCAAA	CGTGAACTAC	31697

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CTGGGTCTAA	AGTATCTGAC	CGAGGCAGTC	CTGTCGCGCA	TTCAACCCGG	TGGTTCGATT	31757
GTCAACGTGT	CCTCTGTGCT	TGGCGCCGAG	TGGCCGGCCC	GCCTTCAGTT	GCATAAGGAG	31817
CTGGGGAGTG	TTGTTGGATT	CTCCGAAGGC	CAGGCATGGC	TTAAGCAGAA	TCCAGTGGCC	31877
CCCGAATTCT	GCTACCAGTA	TTTCAAAGAA	GCACTGATCG	TTTGGTCTCA	AGTTCAGGCG	31937
CAGGAATGGT	TCATGAGGAC	GTCTGTACGC	ATGAACTGCA	TCGCCCCCGG	CCCTGTATTC	31997
ACTCCCATTC	TCAATGAGTT	CGTCACCATG	CTGGGTCAAG	AGCGGACTCA	GGCGGACGCT	32057
CATCGTATTA	AGCGCCCAGC	ATATGCCGAT	GAAGTGGCCG	CGGTGATTGC	ATTCATGTGT	32117
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AAAGGATTCT	TGTGAAGCTT	TAGTTGTCCG	TAAACGAAAA	AAATAAAAT	GAGGAATGAT	32357
ATGAAAGCAA	GTAGATCAGT	CTGCACTTTC	AAAATAGCTA	CCCTGGCAGG	CGCCATTTAT	32417
GCAGCGCTGC	CAATGTCAGC	TGCAAACTCG	ATGCAGCTGG	ATGTAGGTAG	CTCGGATTGG	32477
ACGGTGCGTT	GGGGACAACA	CCCTCAAGTA	TAGCCTTGCC	TCTCGCCTGA	ATGAGCAAGA	32537
CTCAAGTCTG	ACAAATGCGC	CGACTGTCAA	TGGTTATATC	CGGATATTCA	AAGTCAGGGT	32597
GATCGTAACT	TTGACCGGGG	GCTTGGTATC	CAATCGTCTC	GATATTCTGT	CGGAGCTTGA	32657
GTCAGTCGT	GACTGGTTGG	TG				32679

(2) INFORMATION FOR SEQ ID NO: 2:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 284 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Met Ile Ala Ile Thr Gly Ala Ser Gly Gln Leu Gly Arg Leu Thr Ile
1 5 10 15

Glu Ala Leu Leu Lys Arg Leu Pro Ala Ser Glu Ile Ile Ala Leu Val 20 25 30

Arg Asp Pro Asn Lys Ala Gly Asp Leu Thr Ala Arg Gly Ile Val Val 35 40 45

- Arg Gln Ala Asp Tyr Asn Arg Pro Glu Thr Leu His Arg Ala Leu Ile 50 55 60
- Gly Val Asn Arg Leu Leu Ile Ser Ser Ser Glu Val Gly Gln Arg
 65 70 75 80
- Thr Ala Gln His Arg Ala Val Ile Asp Ala Ala Lys Gln Glu Gly Ile $85 \hspace{1cm} 90 \hspace{1cm} 95$
- Glu Leu Leu Ala Tyr Thr Ser Leu Leu His Ala Asp Lys Ser Ala Leu 100 105 110
- Gly Leu Ala Thr Glu His Arg Asp Thr Glu Gln Ala Leu Thr Glu Ser 115 120 125
- Gly Ile Pro His Val Leu Leu Arg Asn Gly Trp Tyr His Glu Asn Tyr 130 135 140
- Thr Ala Gly Ile Pro Val Ala Leu Val His Gly Val Leu Leu Gly Cys 145 150 155 160
- Ala Gln Asp Gly Leu Ile Ala Ser Ala Ala Arg Ala Asp Tyr Ala Glu 165 170 175
- Ala Ala Val Val Leu Thr Gly Glu Asn Gln Ala Gly Arg Val Tyr
 180 185 190
- Glu Leu Ala Gly Glu Pro Ala Tyr Thr Leu Thr Glu Leu Ala Ala Glu 195 200 205
- Val Ala Pro Gln Ala Gly Lys Thr Val Val Tyr Ser Asn Leu Ser Glu 210 215 220
- Ser Asp Tyr Arg Ser Ala Leu Ile Ser Ala Gly Leu Pro Asp Gly Phe 225 230 235 240
- Ala Ala Leu Leu Ala Asp Ser Asp Ala Gly Ala Ala Lys Gly Tyr Leu 245 250 255
- Phe Asp Ser Ser Gly Asp Ser Arg Lys Leu Ile Gly Arg Pro Thr Thr 260 265 270
- Pro Met Ser Glu Ala Ile Ala Ala Ile Gly Arg 275 280
- (2) INFORMATION FOR SEQ ID NO: 3:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1065 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION:1..1062
- (D) OTHER INFORMATION:/product=
 "Vanillinsaeure-O-Demethylase"
 /gene= "vanA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

	TTT Phe								4	8
	GAT Asp								g	6
	CGG Arg								14	14
	CGC Arg								19	92
	TGC Cys 350								24	10
	ATG Met								28	88
	GTA Val								33	36
_	CTG Leu	_							38	34
	GAG Glu								43	32
	CTG Leu 430								4.8	30

	GCC Ala									528
	CGT Arg								_	576
	ATG Met									624
	GAC Asp									672
	AGT Ser 510									720
	TAT Tyr								_	768
	ATC Ile									816
_	CGC Arg									864
	GGT Gly									912
	CAG Gln 590									960
	ATC Ile									1008
	GCA Ala									1056
GCA Ala	TCA Ser	TGA								1065

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(2) INFORMATION FOR SEQ ID NO: 4:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 354 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

Met Phe Pro Lys Asn Ala Trp Tyr Val Ala Cys Thr Pro Asp Glu Ile 1 5 10 15

Ala Asp Lys Pro Leu Gly Arg Gln Ile Cys Asn Glu Lys Ile Val Phe 20 25 30

Tyr Arg Gly Pro Glu Gly Arg Val Ala Ala Val Glu Asp Phe Cys Pro 35 40 45

His Arg Gly Ala Pro Leu Ser Leu Gly Phe Val Arg Asp Gly Lys Leu 50 60

Ile Cys Gly Tyr His Gly Leu Glu Met Gly Cys Glu Gly Lys Thr Leu 65 70 75 80

Ala Met Pro Gly Gln Arg Val Gln Gly Phe Pro Cys Ile Lys Ser Tyr 85 90 95

Ala Val Glu Arg Tyr Gly Phe Ile Trp Val Trp Pro Gly Asp Arg
100 105 110

Glu Leu Ala Asp Pro Ala Leu Ile His His Leu Glu Trp Ala Asp Asn 115 120 125

Pro Glu Trp Ala Tyr Gly Gly Gly Leu Tyr His Ile Ala Cys Asp Tyr 130 135 140

Arg Leu Met Ile Asp Asn Leu Met Asp Leu Thr His Glu Thr Tyr Val 145 150 155 160

His Ala Ser Ser Ile Gly Gln Lys Glu Ile Asp Glu Ala Pro Val Ser 165 170 175

Thr Arg Val Glu Gly Asp Thr Val Ile Thr Ser Arg Tyr Met Asp Asn 180 185 190

Val Met Ala Pro Pro Phe Trp Arg Ala Ala Leu Arg Gly Asn Gly Leu 195 200 205

Ala Asp Asp Val Pro Val Asp Arg Trp Gln Ile Cys Arg Phe Ala Pro 210 215 220

Pro Ser His Val Leu Ile Glu Val Gly Val Ala His Ala Gly Lys Gly 225 230 235 240

Gly Tyr Asp Ala Pro Ala Glu Tyr Lys Ala Gly Ser Ile Val Val Asp
245 250 255

Phe Ile Thr Pro Glu Ser Asp Thr Ser Ile Trp Tyr Phe Trp Gly Met 260 265 270

Ala Arg Asn Phe Arg Pro Gln Gly Thr Glu Leu Thr Glu Thr Ile Arg 275 280 285

Val Gly Gln Gly Lys Ile Phe Ala Glu Asp Leu Asp Met Leu Glu Gln 290 295 300

Gln Gln Arg Asn Leu Leu Ala Tyr Pro Glu Arg Gln Leu Leu Lys Leu 305 310 315 320

Asn Ile Asp Ala Gly Gly Val Gln Ser Arg Arg Val Ile Asp Arg Ile 325 330 335

Leu Ala Ala Glu Gln Glu Ala Ala Asp Ala Ala Leu Ile Ala Arg Ser 340 345 350

Ala Ser

- (2) INFORMATION FOR SEQ ID NO: 5:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 954 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..951
 - (D) OTHER INFORMATION:/product= "Vanillin-O-Demethylase"
 /gene= "vanB"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

ATG ATT GAG GTA ATC ATT TCG GCG ATG CGC TTG GTT GCT CAG GAC ATC

Met Ile Glu Val Ile Ile Ser Ala Met Arg Leu Val Ala Gln Asp Ile

355 360 370

96

ATT AGC CTT GAG TTT GTC CGG GCT GAC GGT GGC TTG CTT CCG CCT GTC Ile Ser Leu Glu Phe Val Arg Ala Asp Gly Gly Leu Leu Pro Pro Val 375 380 385

			CAC His						_	_			144
			TGG Trp		_	_	_	_					192
			GAC Asp										240
_			GTC Val				_	_		_			288
			GAA Glu 455										336
	_		ACG Thr					_	_	_			384
	_		TTC Phe										432
_	_		GAA Glu						_	_		_	480
			GAC Asp										528
_		_	GCC Ala 535										576
			ATG Met										624
	_		CGA Arg	_									672
			GAT Asp										720

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_	GTG Val		_													768
	GCC Ala															816
	TGC Cys															864
	CTC Leu															912
	TCG Ser 660												TAA			954
(2)	INFO	ORMAC	rion	FOR	SEQ	ID 1	10: (5:								
		(E	SEQUE A) LE B) T'	ENGTI (PE:	H: 31 amir	l7 ar no ac	mino cid									
		MOI SEQ				-		SEQ I	D NO	o: 6:	:					
Met 1	Ile	Glu	Val	Ile 5	Ile	Ser	Ala	Met	Arg 10	Leu	Val	Ala	Gln	Asp 15	Ile	
Ile	Ser	Leu	Glu 20	Phe	Val	Arg	Ala	Asp 25	Gly	Gly	Leu	Leu	Pro 30	Pro	Val	
Glu	Ala	Gly 35	Ala	His	Val	Asp	Val 40	His	Leu	Pro	Gly	Gly 45	Leu	Ile	Arg	
Gln	Tyr 50	Ser	Leu	Trp	Asn	Gln 55	Pro	Gly	Ala	Gln	Ser 60	His	Tyr	Cys	Ile	
Gly 65	Val	Leu	Lys	Asp	Pro 70	Ala	Ser	Arg	Gly	Gly 75	Ser	Lys	Ala	Val	His 80	
Glu	Asn	Leu	Arg	Val 85	Gly	Met	Arg	Val	Gln 90	Ile	Ser	Glu	Pro	Arg 95	Asn	
Leu	Phe	Pro	Leu 100	Glu	Glu	Gly	Val	Glu 105	Arg	Ser	Leu	Leu	Phe 110	Ala	Gly	
Gly	Ile	Gly	Ile	Thr	Pro	Ile	Leu	Cys	Met	Ala	Gln	Glu	Leu	Ala	Ala	

Arg Glu Gln Asp Phe Glu Leu His Tyr Cys Ala Arg Ser Thr Asp Arg 130 135 140

Ala Ala Phe Val Glu Trp Leu Lys Val Cys Asp Phe Ala Asp His Val 145 150 155 160

Arg Phe His Phe Asp Asn Gly Pro Asp Gln Gln Lys Leu Asn Ala Ala 165 170 175

Ala Leu Leu Ala Ala Glu Ala Glu Gly Thr His Leu Tyr Val Cys Gly
180 185 190

Pro Gly Gly Phe Met Gly His Val Leu Asp Thr Ala Lys Glu Gln Gly 195 200 205

Trp Ala Asp Asn Arg Leu His Arg Glu Tyr Phe Ala Ala Ala Pro Asn 210 215 220

Val Ser Ala Asp Asp Gly Ser Phe Glu Val Arg Ile His Ser Thr Gly 225 230 235 240

Gln Val Leu Gln Val Pro Ala Asp Gln Thr Val Ser Gln Val Leu Asp 245 250 255

Ala Ala Gly Ile Ile Val Pro Val Ser Cys Glu Gln Gly Ile Cys Gly 260 265 270

Thr Cys Ile Thr Arg Val Val Asp Gly Glu Pro Asp His Arg Asp Phe 275 280 285

Phe Leu Thr Asp Ala Glu Lys Ala Lys Asn Asp Gln Phe Thr Pro Cys 290 295 300

Cys Ser Arg Ala Lys Ser Ala Cys Leu Val Leu Asp Leu 305 310 315

- (2) INFORMATION FOR SEQ ID NO: 7:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1119 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

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(ix) FEATURE:

(A) NAME/KEY: CDS(B) LOCATION:1..1116

(D) OTHER INFORMATION:/product=
 "Formaldehyd-Dehydrogenase"
 /gene= "fdh"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

						CAG Gln			48
						GAA Glu			96
						TAC Tyr		1	L44
						GGT Gly		1	192
						TCG Ser 395		2	240
						CGT Arg		2	288
						GTG Val		3	336
						TTC Phe		3	384
_						TTC Phe		4	132
						AAG Lys 475		4	180
						ACC Thr		,	528

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	GCG Ala 495	_		_		_	_	_			 	 576
	TTC Phe											624
	GCC Ala											 672
	GAT Asp											720
	CAC His											768
	GTG Val 575											816
	GCA Ala											864
	GTG Val											912
	ACC Thr											960
_	ACC Thr					_		_	_	_		1008
	CTG Leu 655											1056
	GCC Ala											1104
	TTG Leu		TAG									1119

(2) INFORMATION FOR SEQ ID NO: 8:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 372 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

Met Ile Lys Ser Arg Ala Ala Val Ala Phe Ala Pro Asn Gln Pro Leu

1 5 10 15

Gln Ile Val Glu Val Asp Val Ala Pro Pro Lys Ala Gly Glu Val Leu 20 25 30

Val Arg Val Val Ala Thr Gly Val Cys His Thr Asp Ala Tyr Thr Leu
35 40 45

Ser Gly Ala Asp Ser Glu Gly Val Phe Pro Cys Ile Leu Gly His Glu 50 55 60

Gly Gly Gly Ile Val Glu Ala Val Gly Glu Gly Val Thr Ser Leu Ala 65 70 75 80

Val Gly Asp His Val Ile Pro Leu Tyr Thr Ala Glu Cys Arg Glu Cys 85 90 95

Lys Phe Phe Lys Ser Gly Lys Thr Asn Leu Cys Gln Lys Val Arg Ala

Thr Gln Gly Lys Gly Leu Met Pro Asp Gly Thr Ser Arg Phe Ser Tyr 115 120 125

Asn Gly Gln Pro Ile Tyr His Tyr Met Gly Cys Ser Thr Phe Ser Glu 130 135 140

Pro Leu Glu Lys Val Cys Leu Leu Gly Cys Gly Val Thr Thr Gly Ile

Gly Ala Val Leu Asn Thr Ala Lys Val Glu Glu Gly Ala Thr Val Ala 180 185 190

Ile Phe Gly Leu Gly Gly Ile Gly Leu Ala Ala Ile Ile Gly Ala Lys
195 200 205

Met Ala Lys Ala Ser Arg Ile Ile Ala Ile Asp Ile Asn Pro Ser Lys 210 215 220

Phe Asp Val Ala Arg Glu Leu Gly Ala Thr Asp Phe Val Asn Pro Asn 225 230 235 240

Asp His Ala Lys Pro Ile Gln Asp Val Ile Val Glu Met Thr Asp Gly 245

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- Gly Val Asp Tyr Ser Phe Glu Cys Ile Gly Asn Val Arg Leu Met Arg 260 265
- Ala Ala Leu Glu Cys Cys His Lys Gly Trp Gly Glu Ser Val Ile Ile 280
- Gly Val Ala Pro Ala Gly Ala Glu Ile Asn Thr Arg Pro Phe His Leu 290 295 300
- Val Thr Gly Arg Val Trp Arg Gly Ser Ala Phe Gly Gly Val Lys Gly
- Arg Thr Glu Leu Pro Ser Tyr Val Glu Lys Ala Gln Gln Gly Glu Ile 325
- Pro Leu Asp Thr Phe Ile Thr His Thr Met Gly Leu Asp Asp Ile Asn 340
- Thr Ala Phe Asp Leu Met Asp Glu Gly Lys Ser Ile Arg Ser Val Val 360

Gln Leu Ser Arg 370

- (2) INFORMATION FOR SEQ ID NO: 9:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1638 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1.. 1635
 - (D) OTHER INFORMATION:/product= "gamma-Glutamylcystein-Synthetase" /gene= "gcs"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

ATG CCG CAA ACT CTT GCT GGA CGG TTG AGT CTG TTA TCC GGC ACC GAC Met Pro Gln Thr Leu Ala Gly Arg Leu Ser Leu Leu Ser Gly Thr Asp 375 380

48

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		ACC Thr									96
		GTC Val									144
_		GGC Gly									192
		CTG Leu									240
		GCT Ala 455	_	_				_			288
		GAG Glu						_		_	336
	_	CAA Gln	_								384
		CAC His	_		_						432
		TGC Cys									480
		GCT Ala 535	_	_	_		_				528
		CAG Gln									576
		TGG Trp									624
		TTC Phe									672

GAT	ACG	CTT	TAC	ATG	ccc	TAT	GCA	ACC	AGC	TTG	CGC	АTG	AGT	GAC	ATC	720
									Ser							
									CTA Leu							768
									CGT Arg							816
									GCA Ala							864
									AGT Ser 670							912
								_	GAG Glu					_		960
									CTG Leu		_					1008
									ACC Thr							1056
									GAG Glu							1104
									TCT Ser 750							1152
															CTC Leu	1200
									ACG Thr						GTG Val	1248
									TCA Ser						TGG Trp	1296
									CCG Pro						GCT Ala 820	1344

CAG Gln	GTG Val	CTC Leu	GCA Ala	GAG Glu 825	ATA Ile	CAC His	AGA Arg	CAC His	GGT Gly 830	GGG Gly	AGC Ser	TTC Phe	ACG Thr	GCA Ala 835	TTT Phe	1392
GGT Gly	CGC Arg	CAA Gln	TTA Leu 840	GCT Ala	ATC Ile	GAC Asp	CAT His	GCA Ala 845	AAA Lys	CAC His	TTC Phe	AGT Ser	GCC Ala 850	TCC Ser	TCG Ser	1440
CTT Leu	GAG Glu	GCT Ala 855	GGC Gly	GTA Val	GCC Ala	AAA Lys	GCG Ala 860	CTT Leu	GAC Asp	CTC Leu	CAG Gln	GCG Ala 865	ACG Thr	TCG Ser	TCT Ser	1488
CTG Leu	CGC Arg 870	GAG Glu	CAG Gln	CAT His	CAA Gln	TTG Leu 875	GAG Glu	GCC Ala	AAC Asn	GAC Asp	CGT Arg 880	GCG Ala	CCA Pro	TTT Phe	TCT Ser	1536
GAC Asp 885	TAC Tyr	CTT Leu	CAG Gln	CAA Gln	TTC Phe 890	TCC Ser	CTG Leu	GCT Ala	TTC Phe	GGT Gly 895	CAA Gln	TCC Ser	GTC Val	GGC Gly	GCC Ala 900	1584
TCT Ser	CGT Arg	GCG Ala	CCC Pro	AAC Asn 905	CCT Pro	ACC Thr	GCG Ala	CAC His	CTC Leu 910	ATC Ile	GAT Asp	CTG Leu	ACC Thr	CCT Pro 915	CCT Pro	1632
GTC Val	AAT															1638

- (2) INFORMATION FOR SEQ ID NO: 10:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 545 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

Met Pro Gln Thr Leu Ala Gly Arg Leu Ser Leu Leu Ser Gly Thr Asp 1 5 10 15

Glu Leu Thr Leu Leu Leu Arg Gly Gly Arg Gly Ile Glu Arg Glu Ala 20 25 30

Leu Arg Val Asp Val Gln Gly Glu Leu Ala Leu Thr Pro His Pro Ala 35 40 45

Ala Leu Gly Ser Ala Leu Thr His Pro Thr Ile Thr Thr Asp Tyr Ala 50 55 60

Glu Ala Leu Leu Glu Leu Ile Thr Arg Pro Ala Thr Asp Cys Ala Gln 65 70 75 80

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Ala Leu Ala Glu Leu Glu Glu Leu His Arg Phe Val His Ser Arg Leu 90 Glu Gly Glu Tyr Leu Trp Asn Leu Ser Met Pro Gly Arg Leu Pro Val 105 Asp Glu Gln Ile Pro Ile Ala Trp Tyr Gly Pro Ser Asn Pro Gly Met 120 Leu Arg His Val Tyr Arg Arg Gly Leu Ala Leu Arg Tyr Gly Lys Arg 135 Met Gln Cys Ile Ala Gly Ile His Tyr Asn Tyr Ser Leu Pro Pro Glu 150 155 Leu Phe Ala Val Leu Thr Lys Ala Glu Val Gly Ser Pro Lys Leu Leu 170 Glu Arg Gln Ser Ala Ala Tyr Met Arg Gln Ile Arg Asn Leu Arg Gln Tyr Gly Trp Leu Leu Ala Tyr Leu Phe Gly Ala Ser Pro Ala Ile Cys 200 Lys Ser Phe Leu Gly Gly Glu Arg Asp Glu Leu Ala Arg Met Gly Gly 210 215 Asp Thr Leu Tyr Met Pro Tyr Ala Thr Ser Leu Arg Met Ser Asp Ile 235 Gly Tyr Arg Asn Arg Ala Met Asp Asp Leu Ser Pro Ser Leu Asn Asp 245 250 Leu Gly Ala Tyr Ile Arg Asp Ile Cys Arg Ala Leu His Thr Pro Asp Ala Gln Tyr Gln Ala Leu Gly Val Phe Ala Gln Gly Glu Trp Arg Gln 280 Leu Asn Ala Asn Leu Leu Gln Leu Asp Ser Glu Tyr Tyr Ala Leu Ala 290 295 Arg Pro Lys Ser Ala Pro Glu Arg Gly Glu Arg Asn Leu Asp Ala Leu 310 315 Ala Arg Arg Gly Val Gln Tyr Val Glu Leu Arg Ala Leu Asp Leu Asp 325 Pro Phe Ser Pro Leu Gly Ile Gly Leu Thr Cys Ala Lys Phe Leu Asp Gly Phe Leu Leu Phe Cys Leu Leu Ser Glu Ala Pro Val Asp Asp Arg

360

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Asn Ala Gln Arg Ser Arg Pro Gly Lys Ser Glu Pro Gly Arg Gln Val 370 380

Arg Ala Ser Pro Gly Leu Lys Leu His Arg Asn Gly Gln Ser Ile Leu 385 390 395 400

Leu Lys Asp Trp Ala Gln Glu Val Leu Thr Glu Val Gln Ala Cys Val
405 410 415

Glu Leu Leu Asp Ser Ala Asn Gly Gly Ser Ser His Ala Leu Ala Trp 420 425 430

Ser Ala Glu Glu Lys Val Leu Asn Pro Asp Cys Ala Pro Ser Ala 435 440 445

Gln Val Leu Ala Glu Ile His Arg His Gly Gly Ser Phe Thr Ala Phe 450 455 460

Gly Arg Gln Leu Ala Ile Asp His Ala Lys His Phe Ser Ala Ser Ser 465 470 475 480

Leu Glu Ala Gly Val Ala Lys Ala Leu Asp Leu Gln Ala Thr Ser Ser 485 490 495

Leu Arg Glu Gln His Gln Leu Glu Ala Asn Asp Arg Ala Pro Phe Ser 500 505 510

Asp Tyr Leu Gln Gln Phe Ser Leu Ala Phe Gly Gln Ser Val Gly Ala 515 520 525

Ser Arg Ala Pro Asn Pro Thr Ala His Leu Ile Asp Leu Thr Pro Pro 530 540

Val 545

(2) INFORMATION FOR SEQ ID NO: 11:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 354 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1...351

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

ATG Met									48
ATC Ile									96
CCT Pro							 	1	44
AAC Asn 595								1	.92
CGC Arg								2	40
GGG Gly								2	88
AAA Lys								3	36
GGA Gly		TGA						3	54

(2) INFORMATION FOR SEQ ID NO: 12:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 117 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

Met Met Asn Val Asn Tyr Lys Ala Val Gly Ala Ser Leu Leu Ala 1 5 10 15

Phe Ile Ser Gln Gly Ala Trp Ala Glu Ser Pro Ala Ala Ser Gly Asn 20 25 30

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Thr Pro Asp Ile Tyr Arg Lys Thr Cys Thr Tyr Cys His Glu Pro Thr 35 40 45

Val	Asn 50	Asn	Gly	Arg	Val	Ile 55	Ala	Arg	Ser	Leu	Gly 60	Pro	Thr	Leu	Arg	
Gly 65	Arg	Gln	Ile	Pro	Pro 70	Gln	Tyr	Thr	Glu	Tyr 75	Met	Val	Arg	His	Gly 80	
Arg	Gly	Ala	Met	Pro 85	Ala	Phe	Ser	Glu	Ala 90	Glu	Val	Pro	Pro	Ala 95	Glu	
Leu	Lys	Val	Leu 100	Gly	Asp	Trp	Ile	Gln 105	Gln	Ser	Ser	Ala	Pro 110	Lys	Asp	
Ala	Gly	Val 115	Ala	Pro												
(2)	INFO	ORMA!	rion	FOR	SEQ	ID 1	10: 1	13:								
	(i)	(<i>I</i> (1	QUENC A) LI B) TY C) SY	engti 1PE : 1RANI	H: 68 nucl DEDNE	87 ba eic ESS:	ase p acid doub	pairs d	5							
	(ii)	MOI	LECUI	LE TY	PE:	AND	(ger	nomi	=)							
	(iii)	HYI	POTHE	ETICA	AL: 1	10										
	(iv)	NA (ri-se	ENSE:	NO											
	(ix)	(<i>P</i>	ATURE A) N. B) LO O) OI	AME/F	: NO	68		:/ger	le= '	'ORF	5"					
	(xi)	SEÇ	QUENC	CE DE	SCRI	PTIC	N: S	SEQ 1	D NO	o: 13	3:					
	ACT Thr															48
	GTG Val 135															96
	CCC Pro															144

		ATG Met				_		 _	_		192
		GTA Val									240
	_	GCA Ala 200									288
		AGG Arg									336
	_	GTG Val									384
		CAC His									432
_		GCC Ala									480
		GCG Ala 280									528
_	_	GCC Ala					_			_	576
		GTG Val									 624
		CTA Leu									672
		GAT Asp	TGA								68°

(2) INFORMATION FOR SEQ ID NO: 14:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 228 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

Met Thr Thr Arg Arg Asn Phe Leu Ile Gly Ala Ser Gln Val Gly Ala 1 5 10 15

Leu Val Met Met Ser Pro Lys Leu Val Phe Arg Thr Pro Leu Lys Gln
20 25 30

Lys Pro Val Arg Ile Leu Ser Thr Gly Leu Ala Gly Glu Glu Phe $35 \hspace{1cm} 40 \hspace{1cm} 45$

His Ser Met Leu Arg Ala Arg Leu Thr His Thr Gly Gln Val Asp Ile 50 55 60

Ala Ser Val Pro Leu Asp Ala Ala Ile Trp Ala Ser Pro Ala Arg Leu 65 70 75 80

Ala Gln Ala Met Asp Ala Leu Asn Gly Thr Arg Leu Ile Ala Phe Val 85 90 95

Glu Pro Arg Asn Glu Leu Ile Leu Met Gln Phe Leu Met Asp Arg Gly 100 105 110

Ala Ala Val Leu Ile Gln Gly Glu His Ala Val Asp Ser Lys Gly Val 115 120 125

Ser Arg His Asp Phe Leu Ser Thr Pro Ser Ser Ala Gly Ile Gly Gly 130 135 140

Ala Leu Ala Asp Ser Leu Ala Lys Gly Gly Ser Pro Phe Ser Ile Ser 145 150 155 160

Val Arg Ala Leu Gly Ser Val Thr Ala Gln Pro Arg Ser Asn Gln Ser 165 170 175

Glu Val Ala Thr His Trp Thr Thr Ala Leu Gly Thr Tyr Tyr Ala Asp 180 185 190

Ile Ala Val Gly Arg Trp Glu Pro Gln Arg Glu Val Ala Ser Tyr Gly
195 200 205

Ser Gly Leu Ile Met Ala Glu Arg Leu Asp Arg Val Ala Ser Thr Phe 210 220

Ile Ala Asp Leu 225

- (2) INFORMATION FOR SEQ ID NO: 15:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1554 base pairs
 - (B) TYPE: nucleic acid

(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

			EATUF (A) N (B) I (D) C	IAME/ LOCAT OTHER UE /g	'ION: C INF G-Eug gene=	11 ORMA enol "eh	.551 ATION -Hyd yB"	lroxy	lase	, rr		opro	tein			
			QUEN													
ATG Met	GAA Glu 230	Ser	ACC Thr	GTA Val	GTT Val	Leu 235	Pro	GAG Glu	GGT Gly	GTC Val	ACC Thr 240	Pro	GAG Glu	CAG Gln	TTC Phe	48
ACC Thr 245	AAA Lys	GCC Ala	: ATC	AGC Ser	GAG Glu 250	Phe	CGT Arg	CAG Gln	GTA Val	TTG Leu 255	GGT Gly	GAG Glu	GAC Asp	AGT Ser	GTT Val 260	96
CTT Leu	GTC Val	ACT Thr	GCT Ala	GAA Glu 265	CGA Arg	GTT Val	GTT Val	CCC Pro	TAT Tyr 270	ACG Thr	AAA Lys	CTC Leu	CTC Leu	ATT Ile 275	CCT Pro	144
ACA Thr	CAG Gln	GAT Asp	GAT Asp 280	GCC Ala	CAG Gln	TAC Tyr	ACC Thr	CCG Pro 285	GCC Ala	GGT Gly	GCC Ala	TTG Leu	ACT Thr 290	CCT Pro	TCT Ser	192
TCG Ser	GTG Val	GAG Glu 295	CAG Gln	GTC Val	CAG Gln	AAA Lys	GTC Val 300	ATG Met	GGG Gly	ATC Ile	TGC Cys	AAT Asn 305	AAG Lys	TAC Tyr	AAG Lys	240
ATC Ile	ccg Pro 310	GTA Val	TGG Trp	CCA Pro	ATC Ile	TCT Ser 315	ACC Thr	GGT Gly	CGG Arg	AAC Asn	TGG Trp 320	GGG Gly	TAT Tyr	GGG Gly	TCC Ser	288
GCT Ala 325	TCG Ser	CCT Pro	GCA Ala	ACT Thr	CCT Pro 330	GGG Gly	CAG Gln	ATG Met	ATT Ile	CTT Leu 335	GAC Asp	CTT Leu	CGC Arg	AAG Lys	ATG Met 340	336
AAC Asn	AAG Lys	ATC Ile	ATT Ile	GAG Glu 345	ATC Ile	GAT Asp	GTT Val	GAG Glu	GGG Gly 350	TGT Cys	ACT Thr	GCC Ala	CTG Leu	CTC Leu 355	GAG Glu	384
CCG Pro	GGC Gly	GTT Val	ACC Thr 360	TAC Tyr	CAG Gln	CAG Gln	CTT Leu	CAC His 365	GAT Asp	TAC Tyr	ATC Ile	AAG Lys	GAG Glu 370	CAC His	AAT Asn	432

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CTG	CCC	TTG	ATG	CTG	GAT	GTG	ccg	ACT	ATT	GGG	CCT	' ATG	GTT	GGC	CCG	480
ьeu	. PIO	375	Met	ьeu	Asp	Val	9ro 380		Ile	Gly	Pro	Met 385		Gly	Pro	
GTG Val	GGT Gly 390	Asn	ACG Thr	CTG Leu	GAT Asp	CGA Arg 395	GGC Gly	GTT Val	GGT Gly	TAT	ACG Thr 400	CCG Pro	TAC Tyr	GGC Gly	GAG Glu	528
CAC	TTC	ATG	ATG	CAG	TGT	GGT	ATG	GAA	GTC	GTC	AТG	GCC	GAT	GGC	GAA	576
405	FIIE	Met	Met	GIN	410	GTÀ	Met	Glu	Va⊥	Val 415	Met	Ala	Asp	Gly	Glu 420	
ATC Ile	CTC Leu	CGT Arg	ACT Thr	GGT Gly 425	ATG Met	GGC Gly	TCG Ser	GTG Val	CCC Pro 430	AAA Lys	GCC Ala	AAG Lys	ACT Thr	TGG Trp 435	CAG Gln	624
GCA Ala	TTC Phe	AAA Lys	TGG Trp 440	GGC Gly	TAT Tyr	GGT Gly	CCA Pro	TAT Tyr 445	CTG Leu	GAC Asp	GGT Gly	ATC Ile	TTT Phe 450	ACC Thr	CAG Gln	672
TCC Ser	AAC Asn	TTT Phe 455	GGT Gly	GTT Val	GTG Val	ACA Thr	AAG Lys 460	CTC Leu	GGG Gly	ATT Ile	TGG Trp	TTG Leu 465	ATG Met	CCC Pro	AAG Lys	720
CCG Pro	CCA Pro 470	GTG Val	ATC Ile	AAG Lys	TCG Ser	TTT Phe 475	ATG Met	ATC Ile	CGT Arg	TAT Tyr	CCC Pro 480	AAT Asn	GAA Glu	GCT Ala	GAT Asp	768
GTG Val 485	GTT Val	AAG Lys	GCA Ala	ATT Ile	GAT Asp 490	GCT Ala	TTT Phe	CGC Arg	CCG Pro	CTG Leu 495	CGT Arg	ATT Ile	ACT Thr	CAG Gln	CTG Leu 500	816
ATT Ile	CCT Pro	AAC Asn	GTC Val	GTT Val 505	TTG Leu	TTC Phe	ATG Met	CAC His	GGC Gly 510	ATG Met	TAC Tyr	GAA Glu	ACG Thr	GCA Ala 515	ATC Ile	864
TGC Cys	CGG Arg	ACG Thr	CGT Arg 520	GCT Ala	GAG Glu	GTT Val	ACT Thr	TCG Ser 525	GAC Asp	CCA Pro	GGT Gly	CCT Pro	ATT Ile 530	TCT Ser	GAA Glu	912
GCG Ala	GAC Asp	GCC Ala 535	CGC Arg	AAA Lys	GCA Ala	TTC Phe	AAA Lys 540	GAG Glu	CTA Leu	GGC Gly	GTT Val	GGC Gly 545	TAC Tyr	TGG Trp	AAC Asn	960
GTT Val	TAC Tyr 550	TTC Phe	GCG Ala	CTT Leu	TAC Tyr	GGC Gly 555	ACA Thr	GAA Glu	GAG Glu	CAG Gln	ATA Ile 560	GCC Ala	GTC Val	AAT Asn	GAA Glu	1008
AAG Lys 565	ATC Ile	GTC Val	CGC Arg	GGC GLy	ATC Ile 570	CTC Leu	GAA Glu	CCG Pro	Thr	GGG Gly 575	GGT Gly	GAG Glu	ATC Ile	CTC Leu	ACC Thr 580	1056

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GAA Glu	. GAG Glu	GAG Glu	GCT Ala	GGA Gly 585	Asp	AAC Asn	ATT Ile	CTT Leu	TTC Phe 590	CAT His	CAC His	CAT His	AAG Lys	CAG Gln 595	CTC Leu		1104
ATG Met	AAC Asn	GGC Gly	GAG Glu 600	Met	ACA Thr	TTG Leu	GAG Glu	GAA Glu 605	Met	AAT Asn	ATC Ile	TAC Tyr	CAG Gln 610	TGG Trp	CGC Arg		1152
GGA Gly	GCA Ala	GGT Gly 615	Gly	GGT Gly	GCT Ala	TGC Cys	TGG Trp 620	TTT Phe	GCA Ala	CCG Pro	GTT Val	GCT Ala 625	CAG Gln	GTC Val	AAG Lys		1200
GGG Gly	CAT His 630	GAG Glu	GCA Ala	GAG Glu	CAG Gln	CAG Gln 635	GTC Val	AAG Lys	CTT Leu	GCT Ala	CAG Gln 640	AAG Lys	GTG Val	CTT Leu	GCA Ala		1248
AAG Lys 645	CAT His	GGG Gly	TTC Phe	GAT Asp	TAC Tyr 650	ACG Thr	GCG Ala	GGC Gly	TTT Phe	GCG Ala 655	ATT Ile	GGT Gly	TGG Trp	CGC Arg	GAT Asp 660		1296
CTT Leu	CAC His	CAT His	GTG Val	ATC Ile 665	GAT Asp	GTG Val	CTG Leu	TAC Tyr	GAC Asp 670	CGT Arg	AGC Ser	AAT Asn	GCC Ala	GAC Asp 675	GAG Glu	:	1344
AAA Lys	AAG Lys	CGC Arg	GCT Ala 680	TAC Tyr	GCT Ala	TGC Cys	TTT Phe	GAT Asp 685	GAA Glu	TTG Leu	ATC Ile	GAC Asp	GTC Val 690	TTT Phe	GCG Ala	:	1392
GCC Ala	GAA Glu	GGC Gly 695	TTT Phe	GCA Ala	AGT Ser	TAC Tyr	AGG Arg 700	ACC Thr	AAT Asn	ATT Ile	GCC Ala	TTT Phe 705	ATG Met	GAC Asp	AAA Lys	3	1440
GTC Val	GCC Ala 710	TCT Ser	AAG Lys	TTC Phe	GGC Gly	GCT Ala 715	GAG Glu	AAT Asn	AAG Lys	AGG Arg	GTC Val 720	AAT Asn	CAG Gln	AAG Lys	ATC Ile	1	1488
AAG Lys 725	GCT Ala	GCC Ala	CTT Leu	GAT Asp	CCA Pro 730	AAC Asn	GGC Gly	ATC Ile	ATC Ile	GCT Ala 735	CCC Pro	GGC Gly	AAG Lys	TCG Ser	GGC Gly 740	1	L536
ATT Ile					AAT											1	L554

(2) INFORMATION FOR SEQ ID NO: 16:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 517 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

Met Glu Ser Thr Val Val Leu Pro Glu Gly Val Thr Pro Glu Gln Phe Thr Lys Ala Ile Ser Glu Phe Arg Gln Val Leu Gly Glu Asp Ser Val Leu Val Thr Ala Glu Arg Val Val Pro Tyr Thr Lys Leu Leu Ile Pro Thr Gln Asp Asp Ala Gln Tyr Thr Pro Ala Gly Ala Leu Thr Pro Ser Ser Val Glu Gln Val Gln Lys Val Met Gly Ile Cys Asn Lys Tyr Lys Ile Pro Val Trp Pro Ile Ser Thr Gly Arg Asn Trp Gly Tyr Gly Ser 85 Ala Ser Pro Ala Thr Pro Gly Gln Met Ile Leu Asp Leu Arg Lys Met 100 105 Asn Lys Ile Ile Glu Ile Asp Val Glu Gly Cys Thr Ala Leu Leu Glu 120 Pro Gly Val Thr Tyr Gln Gln Leu His Asp Tyr Ile Lys Glu His Asn 135 Leu Pro Leu Met Leu Asp Val Pro Thr Ile Gly Pro Met Val Gly Pro 150 155 Val Gly Asn Thr Leu Asp Arg Gly Val Gly Tyr Thr Pro Tyr Gly Glu 170 His Phe Met Met Gln Cys Gly Met Glu Val Val Met Ala Asp Gly Glu Ile Leu Arg Thr Gly Met Gly Ser Val Pro Lys Ala Lys Thr Trp Gln 200 Ala Phe Lys Trp Gly Tyr Gly Pro Tyr Leu Asp Gly Ile Phe Thr Gln Ser Asn Phe Gly Val Val Thr Lys Leu Gly Ile Trp Leu Met Pro Lys Pro Pro Val Ile Lys Ser Phe Met Ile Arg Tyr Pro Asn Glu Ala Asp 245 250 Val Val Lys Ala Ile Asp Ala Phe Arg Pro Leu Arg Ile Thr Gln Leu Ile Pro Asn Val Val Leu Phe Met His Gly Met Tyr Glu Thr Ala Ile 280

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Cys	Arg 290	Thr	Arg	Ala	Glu	Val 295	Thr	Ser	Asp	Pro	Gly 300	Pro	Ile	Ser	Glu
Ala 305	Asp	Ala	Arg	Lys	Ala 310	Phe	Lys	Glu	Leu	Gly 315	Val	Gly	Tyr	Trp	Asr 320
Val	Tyr	Phe	Ala	Leu 325	Tyr	Gly	Thr	Glu	Glu 330	Gln	Ile	Ala	Val	Asn 335	Glu
Lys	Ile	Val	Arg 340	Gly	Ile	Leu	Glu	Pro 345	Thr	Gly	Gly	Glu	Ile 350	Leu	Thr
Glu	Glu	Glu 355	Ala	Gly	Asp	Asn	Ile 360	Leu	Phe	His	His	His 365	Lys	Gln	Let
Met	Asn 370	Gly	Glu	Met	Thr	Leu 375	Glu	Glu	Met	Asn	Ile 380	Tyr	Gln	Trp	Arç
Gly 385	Ala	Gly	Gly	Gly	Ala 390	Cys	Trp	Phe	Ala	Pro 395	Val	Ala	Gln	Val	Lys 400
Gly	His	Glu	Ala	Glu 405	Gln	Gln	Val	Lys	Leu 410	Ala	Gln	Lys	Val	Leu 415	Ala
Lys	His	Gly	Phe 420	Asp	Tyr	Thr	Ala	Gly 425	Phe	Ala	Ile	Gly	Trp 430	Arg	Asp
Leu	His	His 435	Val	Ile	Asp	Val	Leu 440	Tyr	Asp	Arg	Ser	Asn 445	Ala	Asp	Glı
Lys	Lys 450	Arg	Ala	Tyr	Ala	Cys 455	Phe	Asp	Glu	Leu	Ile 460	Asp	Val	Phe	Ala
Ala 465	Glu	Gly	Phe	Ala	Ser 470	Tyr	Arg	Thr	Asn	Ile 475	Ala	Phe	Met	Asp	Lу:
Val	Ala	Ser	Lys	Phe 485	Gly	Ala	Glu	Asn	Lys 490	Arg	Val	Asn	Gln	Lys 495	Ιlϵ
Lys	Ala	Ala	Leu 500	Asp	Pro	Asn	Gly	Ile 505	Ile	Ala	Pro	Gly	Lys 510	Ser	Gly

515

Ile His Leu Pro Lys

(i) SEQUENCE CHARACTERISTICS:

(2) INFORMATION FOR SEQ ID NO: 17:

- (A) LENGTH: 861 base pairs
- (A) mandin: our base pe
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)

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48 Met Ile Ala Ile Thr Ala Gly Thr Gly Ser Leu Gly Arg Ala Ile Val GAG CGA CTA GGG GAC TGC GGT CTT ATC GGT CAA GTT CGA TTG ACG GCT 96 Glu Arg Leu Gly Asp Cys Gly Leu Ile Gly Gln Val Arg Leu Thr Ala CGC GAT CCT AAA AGG CTT CGT GCC GCT GCC GAG GAA GGG TTT CAG GTC 144 Arg Asp Pro Lys Arg Leu Arg Ala Ala Ala Glu Glu Gly Phe Gln Val GCT AAG GCG GAT TAC GCC GAT ATT GGG AGT CTT GAC CAG GCA TTA CAG 192 Ala Lys Ala Asp Tyr Ala Asp Ile Gly Ser Leu Asp Gln Ala Leu Gln 570 GGG GTA GAC GTA TTA CTC CTG ATT TCT GGT ACT GCA CCC AAT GAA ATA 240 Gly Val Asp Val Leu Leu Ile Ser Gly Thr Ala Pro Asn Glu Ile 585 590 AGG ATC CAA CAG CAT AAG TCG GTC ATC GAC GCG GCA AAA CGA AAC GGC 288 Arg Ile Gln Gln His Lys Ser Val Ile Asp Ala Ala Lys Arg Asn Gly 605 GTG TCG CGT ATT GTG TAT ACC AGC TTC ATA AAT CCA AGT ACT CGC AGC 336 Val Ser Arg Ile Val Tyr Thr Ser Phe Ile Asn Pro Ser Thr Arg Ser 620 AGG TCT ATT TGG GCC TCC ATT CAT CGT GAA ACT GAG ACT TAC CTC AGG 384 Arg Ser Ile Trp Ala Ser Ile His Arg Glu Thr Glu Thr Tyr Leu Arg 635 CAG TCT GGG GTG AAG TTT ACG ATT GTC CGA AAT AAT CAG TAT GCG TCT 432 Gln Ser Gly Val Lys Phe Thr Ile Val Arg Asn Asn Gln Tyr Ala Ser 650 AAC CTG GAT CTG TTG CTG AGG GCT CAA GAC AGC GGA ATA TTT GCC 480 Asn Leu Asp Leu Leu Leu Arg Ala Gln Asp Ser Gly Ile Phe Ala 665 670

	CCC Pro												528
	GCT Ala 695											_	576
	TAC Tyr												624
	ATT Ile												672
	CCT Pro												720
	ATG Met		GAA				ATT				GGT		768
	TAC Tyr 775	CAA				GAT				ACG			816
	GAA Glu				TAC				GTT				858
TGA				193				500					861

- (2) INFORMATION FOR SEQ ID NO: 18:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 286 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

Met Ile Ala Ile Thr Ala Gly Thr Gly Ser Leu Gly Arg Ala Ile Val 1 5 10 15

Glu Arg Leu Gly Asp Cys Gly Leu Ile Gly Gln Val Arg Leu Thr Ala 20 25 30

Arg Asp Pro Lys Arg Leu Arg Ala Ala Ala Glu Glu Gly Phe Gln Val 35 40 45

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- Ala Lys Ala Asp Tyr Ala Asp Ile Gly Ser Leu Asp Gln Ala Leu Gln 50 55 60
- Gly Val Asp Val Leu Leu Leu Ile Ser Gly Thr Ala Pro Asn Glu Ile
 65 70 75 80
- Arg Ile Gln Gln His Lys Ser Val Ile Asp Ala Ala Lys Arg Asn Gly
 85 90 95
- Val Ser Arg Ile Val Tyr Thr Ser Phe Ile Asn Pro Ser Thr Arg Ser 100 105 110
- Arg Ser Ile Trp Ala Ser Ile His Arg Glu Thr Glu Thr Tyr Leu Arg 115 120 125
- Gln Ser Gly Val Lys Phe Thr Ile Val Arg Asn Asn Gln Tyr Ala Ser 130 135 140
- Asn Leu Asp Leu Leu Leu Leu Arg Ala Gln Asp Ser Gly Ile Phe Ala 145 150 155 160
- Ile Pro Gly Ala Lys Gly Arg Val Ala Tyr Val Ser His Arg Asp Val
 165 170 175
- Ala Ala Ile Cys Ser Val Leu Thr Thr Ala Gly His Asp Asn Arg 180 185 190
- Ile Tyr Gln Leu Thr Gly Ser Glu Ala Leu Asn Gly Leu Glu Ile Ala 195 200 205
- Glu Ile Leu Gly Gly Val Leu Gly Arg Pro Val Arg Ala Met Asp Ala 210 215 220
- Ser Pro Asp Glu Phe Ala Ala Ser Phe Arg Glu Ala Gly Phe Pro Glu 225 230 235 240
- Phe Met Val Glu Gly Leu Leu Ser Ile Tyr Ala Ala Ser Gly Ala Gly 245 250 255
- Glu Tyr Gln Ser Val Ser Pro Asp Val Gly Leu Leu Thr Gly Arg Arg 260 265 270
- Ala Glu Ser Met Arg Thr Tyr Ile Gln Arg Leu Val Trp Pro 275 280 285
- (2) INFORMATION FOR SEQ ID NO: 19:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1011 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

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								-	- 74 -						
(iii)	HYI	POTHI	ETIC	AL: 1	10										
(iv)	NA	ri-si	ENSE	: NO											
, ,	(B) L(AME/I OCATI THER	ION: INFO	l10 DRMAI "adl	rion: 1"	-				nol-I	Dehyd	droge	enase"	
AAG Lys	GCT	TAT	GAG	CTT	CAC	AAG	ATT	TCG	GAA	CAG					
CAG Gln															
AGG Arg 320															

(xi) SEQU	JENCE DESCRIPTI	ON: SEQ ID N	0: 19:	
Met Lys Ala T			GAA CAG GTA GAG Glu Gln Val Glu 300	
			AAT CAT GGC GAG Asn His Gly Glu 315	
		Leu Asn Phe	CGC GAT TTG ATG Arg Asp Leu Met 330	
			GAT GTG ATC CCG Asp Val Ile Pro 345	
			CCT GGC GTA TCT Pro Gly Val Ser	
Val Gln Gly G			TTC CCT AAC TGG Phe Pro Asn Trp 380	
_			TCG TTG GGC TTC Ser Leu Gly Phe 395	
		Val Ala Leu	CCC TAT GAG GCA Pro Tyr Glu Ala 410	
			GCT GCA ACA TTG Ala Ala Thr Leu 425	
			GAA GTG GGG CGT Glu Val Gly Arg	

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_			Thr					Gly						ATG Met		528
ccc	mmc	CT C	450	cac	מ מ מ	CITIC.	mmc	455	ccc	n.c.c	Cm C	T) (THE	460	7.00	mac	F.7.6
														ACC Thr		576
	Ser					Glu								GAT Asp		624
	480					485					490					
														CTG Leu		672
														GGG Gly 525		720
														ATT Ile		768
														TTG Leu		816
														TCC Ser		864
														ATC Ile	_	912
	_													GCT Ala 605		960
														ACG Thr		1008
TAA																1011

(2) INFORMATION FOR SEQ ID NO: 20:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 336 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

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- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

Met Lys Ala Tyr Glu Leu His Lys Ile Ser Glu Gln Val Glu Val Arg

1 5 10 15

Leu Gln Pro Thr Arg Pro Arg Pro Gln Leu Asn His Gly Glu Val Leu 20 25 30

Ile Arg Val His Ala Ala Ser Leu Asn Phe Arg Asp Leu Met Ile Leu $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$

Ala Gly Arg Tyr Pro Gly Gln Met Lys Pro Asp Val Ile Pro Leu Ser 50 55 60

Asp Gly Ala Gly Glu Ile Val Glu Val Gly Pro Gly Val Ser Ser Glu 65 70 75 80

Val Gln Gly Gln Arg Val Ala Ser Thr Phe Phe Pro Asn Trp Arg Ala 85 90 95

Gly Lys Ile Thr Glu Pro Ala Ile Glu Val Ser Leu Gly Phe Gly Met $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110$

Asp Gly Met Leu Ala Glu Tyr Val Ala Leu Pro Tyr Glu Ala Thr Ile 115 120 125

Pro Ile Pro Glu His Leu Ser Tyr Glu Glu Ala Ala Thr Leu Pro Cys 130 135 140

Ala Ala Leu Thr Ala Trp Asn Ala Leu Thr Glu Val Gly Arg Val Lys
145 150 155 160

Ala Gly Asp Thr Val Leu Leu Leu Gly Thr Gly Gly Val Ser Met Phe 165 170 175

Ala Leu Gln Phe Ala Lys Leu Leu Gly Ala Thr Val Ile His Thr Ser 180 185 190

Ser Ser Glu Gln Lys Leu Glu Arg Val Lys Ala Met Gly Ala Asp His 195 200 205

Leu Ile Asn Tyr Arg Asn Ser Pro Gly Trp Asp Arg Thr Val Leu Asp 210 215 220

Leu Thr Ala Gly Arg Gly Val Asp Leu Val Val Glu Val Gly Gly Ala 225 230 235 240

Gly Thr Leu Glu Arg Ser Leu Arg Ala Val Lys Val Gly Gly Ile Val

Ala Thr Ile Gly Leu Val Ala Gly Val Gly Pro Ile Asp Pro Leu Pro 260 265 270

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Glu Tyr Met Arg Ser Gly Asn His Leu Gly Lys Val Val Ile Thr Ile 325 330 335

(2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1518 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: complement (4..1518)
- (D) OTHER INFORMATION:/product=
 "Lignostilben-Dioxygenase"
 /gene= "lsd"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

60 TCACCGTCGT GATCGGGATT GGAAATTCGT GCGAGGACAG CGGCCACGTA CCGGCGCCCT GAAGGGCTGG AAGGTTGGAG TTTCGTTAAG GTCTGGTACC CAGCAGCCAT GGAGAGCGGC 120 CCTTAGCCGG AATGGCAGCT TGATGGTTGC CACGGGACCA GACTGGATGT CTTGAGTGTC 180 GAGAATTACC AGATCGCTGC GATTTTCATC GAGGCGACCA ACCACGGTCA GCAAGTACCC 240 GTCACCTTCG GCGGCGGTCG GACTTCTAGG GACGAAGGCC GGCTCCTGGG CCGCCGAGGC 300 TTCGCCGGAG TACCAGAGGT CGTAGTCACC TCGGTGGTTG TCCCAGATGC CGAGTGAGTT 360 GTACGCGAAT ATCTTCTCGG CCTGCTGATG CGCAAGTGGT TTGCGTGGAT CGTCCACCCC 420 CATAAAGCCA TAGCGGTTGC ATTGCAGGGC GAACGAAGAA TCCATGATTG GCATTTCCGC 480 AAAGAAATCG TGTAGCCGGG TTCGCTTGAT CTCGTCGCTG CTGCTATCGA GGTCAATTTC 540

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CCAACGAGTC	AGGCGTGGTA	CGGCTTTCTC	AGGGGCGAAG	GGTTGGTTTT	GTGAGTTGGG	600
GAAGGGGAAC	GGCAGGATTT	CACTTTCCAT	AAGGTCGATA	TAAATCTTGG	TTCCGACTTC	660
CCAAGCATTC	ACAACATGAA	ATACCCAGAG	CGCCGGTGCC	TTGAGCCAGC	GAATCAGACT	720
GCCCTGGCGC	GGCGCGAGTA	CGCCAATGTA	GCTGCCCAGT	TCCGGCTCCC	ACATATAAAT	780
TGGCTGTTTC	GCCTTGAGGC	GGGACAGGCT	GTTGGTGGCC	GGCATAATTG	GGAAAATGGA	840
CCAATTTCGG	GTAATGGCAA	AGTCGTGCAT	GAATGCGCCA	TAGGGCTGCT	CAAACCAAGT	900
TTCATGTGTC	ACCTTGCCGT	GCTTGTCGAC	AATGTAATAG	GCCATGTCTG	GAGTTGCTTC	960
GCCCTTAGCT	GCCGAACCGA	AGAACAACAA	GTCACCCGTT	TCCGGGTCAT	ATTTTGGATG	1020
GGCGGTGTGG	GTTTGGCTGG	TAACTTGGCC	GTCGTAGTCG	AAGTGTCCGC	GAGTTTCAAG	1080
TGTACGAGGA	TCCAGTTCGT	ACGGTAGGCC	GTCTTCCTTC	ACCGCCAGCA	CCTTGCCGTG	1140
ATGGCTAATG	ATGCTTGTAT	TGGCAACGGT	GCGGTCTAGT	CCTTTTACAC	TGGTGTCGTC	1200
GGTATAGGGG	TTTCTGTACA	TGCCAAATAG	CGATTTTCGC	GCTAGTCGTT	CGGCCGTGAA	1260
TCGAGCGGTT	TTAACCCAGC	GACTGATGAA	GTCGACATGA	CCATCTTCGA	AGTGGAAGGC	1320
AGAGGCCATT	CCATCTCCAT	CTATGAAGGT	GTGGAATTTT	TGTGGGGTAA	CTTGAGGCTC	1380
TGGCGTATTA	CGGTAGAACG	TTCCATTTAT	TGATTTTGGG	ATTTCGCCGT	CAACCTCTAG	1440
ATCGAACAAG	TCTGCCTCTA	TACGGGTGGG	GAGAAGTGTT	CCTACTAATT	GCGGGTCGTT	1500
CCCCTTCDDT	$CTCCCC\DeltaT$					1519

(2) INFORMATION FOR SEQ ID NO: 22:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 505 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

Met Ala Arg Phe Asn Arg Asn Asp Pro Gln Leu Val Gly Thr Leu Leu 1 5 10 15

Pro Thr Arg Ile Glu Ala Asp Leu Phe Asp Leu Glu Val Asp Gly Glu 20 25 30

Ile Pro Lys Ser Ile Asn Gly Thr Phe Tyr Arg Asn Thr Pro Glu Pro 35 40 45

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Gln	Val 50	Thr	Pro	Gln	Lys	Phe 55	His	Thr	Phe	Ile	Asp 60	Gly	Asp	Gly	Met
Ala 65	Ser	Ala	Phe	His	Phe 70	Glu	Asp	Gly	His	Val 75	Asp	Phe	Ile	Ser	Arg 80
Trp	Val	Lys	Thr	Ala 85	Arg	Phe	Thr	Ala	Glu 90	Arg	Leu	Ala	Arg	Lys 95	Ser
Leu	Phe	Gly	Met 100	Tyr	Arg	Asn	Pro	Tyr 105	Thr	Asp	Asp	Thr	Ser 110	Val	Lys
Gly	Leu	Asp 115	Arg	Thr	Val	Ala	Asn 120	Thr	Ser	Ile	Ile	Ser 125	His	His	Gly
Lys	Val 130	Leu	Ala	Val	Lys	Glu 135	Asp	Gly	Leu	Pro	Tyr 140	Glu	Leu	Asp	Pro
Arg 145	Thr	Leu	Glu	Thr	Arg 150	Gly	His	Phe	Asp	Tyr 155	Asp	Gly	Gln	Val	Thr 160
Ser	Gln	Thr	His	Thr 165	Ala	His	Pro	Lys	Tyr 170	Asp	Pro	Glu	Thr	Gly 175	Asp
Leu	Leu	Phe	Phe 180	Gly	Ser	Ala	Ala	Lys 185	Gly	Glu	Ala	Thr	Pro 190	Asp	Met
Ala	Tyr	Tyr 195	Ile	Val	Asp	Lys	His 200	Gly	Lys	Val	Thr	His 205	Glu	Thr	Trp
Phe	Glu 210	Gln	Pro	Tyr	Gly	Ala 215	Phe	Met	His	Asp	Phe 220	Ala	Ile	Thr	Arg
Asn 225	Trp	Ser	Ile	Phe	Pro 230	Ile	Met	Pro	Ala	Thr 235	Asn	Ser	Leu	Ser	Arg 240
Leu	Lys	Ala	Lys	Gln 245	Pro	Ile	Tyr	Met	Trp 250	Glu	Pro	Glu	Leu	Gly 255	Ser
Tyr	Ile	Gly	Val 260	Leu	Ala	Pro	Arg	Gln 265	Gly	Ser	Leu	Ile	Arg 270	Trp	Leu
Lys	Ala	Pro 275	Ala	Leu	Trp	Val	Phe 280	His	Val	Val	Asn	Ala 285	Trp	Glu	Val
Gly	Thr 290		Ile	Tyr	Ile	Asp 295	Leu	Met	Glu	Ser	Glu 300	Ile	Leu	Pro	Phe
Pro 305	Phe	Pro	Asn	Ser	Gln 310	Asn	Gln	Pro	Phe	Ala 315	Pro	Glu	Lys	Ala	Val 320
Pro	Arg	Leu	Thr	Arg 325	Trp	Glu	Ile	Asp	Leu 330	Asp	Ser	Ser	Ser	Asp 335	Glu

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Ile Lys Arg Thr Arg Leu His Asp Phe Phe Ala Glu Met Pro Ile Met 340 345 350

Asp Ser Ser Phe Ala Leu Gln Cys Asn Arg Tyr Gly Phe Met Gly Val 355 360 365

Asp Asp Pro Arg Lys Pro Leu Ala His Gln Gln Ala Glu Lys Ile Phe 370 375 380

Ala Tyr Asn Ser Leu Gly Ile Trp Asp Asn His Arg Gly Asp Tyr Asp 385 390 395 400

Leu Trp Tyr Ser Gly Glu Ala Ser Ala Ala Gln Glu Pro Ala Phe Val $405 \hspace{1.5cm} 410 \hspace{1.5cm} 415$

Pro Arg Ser Pro Thr Ala Ala Glu Gly Asp Gly Tyr Leu Leu Thr Val 420 425 430

Val Gly Arg Leu Asp Glu Asn Arg Ser Asp Leu Val Ile Leu Asp Thr 435 440 445

Gln Asp Ile Gln Ser Gly Pro Val Ala Thr Ile Lys Leu Pro Phe Arg 450 455 460

Leu Arg Ala Ala Leu His Gly Cys Trp Val Pro Asp Leu Asn Glu Thr 465 470 475 480

Pro Thr Phe Gln Pro Phe Arg Ala Pro Val Arg Gly Arg Cys Pro Arg
485 490 495

Thr Asn Phe Gln Ser Arg Ser Arg Arg 500 505

- (2) INFORMATION FOR SEQ ID NO: 23:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 951 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1...948
 - (D) OTHER INFORMATION:/gene= "ORF3"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

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ATG Met	ACA Thr	ACT Thr	ATT Ile	CGG Arg 510	TGG Trp	CGG Arg	CGT Arg	ATG Met	TCC Ser 515	ATT Ile	CAC His	TCT Ser	GAG Glu	GGG Gly 520	ATC Ile	48
				TCG Ser												96
				TTC Phe												144
				TCT Ser												192
				GTA Val												240
				AGC Ser 590												288
				GGA Gly												336
				cgc Arg												384
				ATA Ile												432
															GGG Gly 665	480
															CGC Arg	528
				Gly					Gly					Val	GCT Ala	576
			ser					Ala					Asp		GGT Gly	624

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										AGA Arg						672
										GTT Val 740						720
										GCT Ala						768
										GGC Gly						816
										CTG Leu						864
										AAG Lys						912
	Gly									CAG Gln 820		TGA				951
(2)		(i) ((SEQU A) L B) T D) T	FOR ENCE ENGT YPE: OPOL LE T	CHA H: 3 ami: OGY:	RACTI 16 ai no a lin	ERIS mino cid ear	TICS aci								
									ID N	0: 2	4:					
Met 1		Thr	Ile	Arg 5	Trp	Arg	Arg	Met	Ser 10		His	Ser	Glu	Gly 15	Ile	
Thr	Leu	Ala	Asp 20		Pro	Leu	His	Trp 25		His	Thr	Leu	Asn 30		ser Ser	
Met	Arg	Thr 35		Phe	Glu	Val	Gln 40		Leu	Glu	Arg	Gly 45		Gly	Ala	
Ser	Leu 50		a Arg	Ser	Arg	Phe 55		Ala	Gly	Glu	Leu 60		Ser	Ala	ı Ile	
Ala		Sei	Glr.	val	Leu 70		His	Phe	e Asr	Asp		Arg	, Asr	n Ala	Asp 80	

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Glu Ala Glu His Ser Tyr Leu Ile Gln Ile Arg Ser Gly Ala Leu Gly
85 90 95

Val Ala Ser Gly Gly Arg Lys Val Ile Leu Ala Asn Gly Asp Cys Ser 100 105 110

Ile Val Asp Ser Arg Gln Asp Phe Thr Leu Ser Ser Asn Ser Ser Thr 115 120 125

Gln Gly Val Val Ile Arg Phe Pro Val Ser Trp Leu Gly Ala Trp Val 130 135 140

Ser Asn Pro Glu Asp Leu Ile Ala Arg Arg Val Asp Ala Glu Val Gly 145 150 155 160

Trp Gly Arg Ala Leu Ser Ala Ser Val Ser Asn Leu Asp Pro Leu Arg 165 170 175

Ile Asp Asp Leu Gly Ser Asn Val Asn Gly Ile Ala Glu His Val Ala 180 185 190

Met Leu Ile Ser Leu Ala Ser Ser Ala Val Ser Ser Glu Asp Gly Gly
195 200 205

Val Ala Leu Arg Lys Met Arg Glu Val Lys Arg Val Leu Glu Gln Ser 210 215 220

Phe Ala Asp Ala Asn Leu Gly Pro Glu Ser Val Ser Ser Gln Leu Gly 225 230 235 240

Ile Ser Lys Arg Tyr Leu His Tyr Val Phe Ala Ala Cys Gly Thr Thr 245 250 255

Phe Gly Arg Glu Leu Leu Glu Ile Arg Leu Gly Lys Ala Tyr Arg Met 260 265 270

Leu Cys Ala Ala Ser Asp Ser Gly Ala Val Leu Lys Val Ala Met Ser 275 280 285

Ser Gly Phe Ser Asp Ser Ser His Phe Ser Lys Lys Phe Lys Glu Arg 290 295 300

Tyr Gly Val Ser Pro Val Ser Leu Val Arg Gln Ala 305 310 315

- (2) INFORMATION FOR SEQ ID NO: 25:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 735 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

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(iii)	HYPOTHETICAL:	NO
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(iv) ANTI-SENSE: NO

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1...732
- (D) OTHER INFORMATION:/product= "Enoyl-CoA-Hydratase" /gene= "ech"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

								GAG Glu 330		48
								GCA Ala		96
	_	_	_			_		GAG Glu		144
								GCG Ala		192
								ATC Ile		240
								GTG Val 410		288
								TCC Ser		336
								ATG Met		384
								GGC Gly		432
								CAG Gln		480

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	CTG Leu															528
	GAC Asp															576
	TGC Cys 510															624
	CTC Leu															672
	ATG Met															720
	TAC Tyr			TGA												735
(2)	(ii)	(i) S (<i>I</i>	SEQUE A) LE B) TY D) TO	ENCE ENGTH PE: OPOLO	CHAI H: 24 amir OGY:	RACTE 14 am no ac line prot	ERIST mino cid ear	FICS:	ds): 26	ō :					
Met 1	Ser	Pro	Thr	Leu 5	Asn	Arg	Glu	Met	Val 10	Glu	Val	Leu	Glu	Val 15	Leu	
Glu	Gln	Asp	Ala 20	Asp	Ala	Arg	Val	Leu 25	Val	Leu	Thr	Gly	Ala 30	Gly	Glu	
Ser	Trp	Thr 35	Ala	Gly	Met	Asp	Leu 40	Lys	Glu	Tyr	Phe	Arg 45	Glu	Thr	Asp	
Ala	Gly 50	Pro	Glu	Ile	Leu	Gln 55	Glu	Lys	Ile	Arg	Arg 60	Glu	Ala	Ser	Thr	
Trp 65	Gln	Trp	Lys	Leu	Leu 70	Arg	Met	Tyr	Thr	Lys 75	Pro	Thr	Ile	Ala	Met 80	
Val	Asn	Gly	Trp	Cys 85	Phe	Gly	Gly	Gly	Phe 90	Ser	Pro	Leu	Val	Ala 95	Cys	
Asp	Leu	Ala	Ile 100	Cys	Ala	Asp	Glu	Ala 105	Thr	Phe	Gly	Leu	Ser 110	Glu	Ile	

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Asn Trp Gly Ile Pro Pro Gly Asn Leu Val Ser Lys Ala Met Ala Asp 115 120 125

Thr Val Gly His Arg Glu Ser Leu Tyr Tyr Ile Met Thr Gly Lys Thr 130 135 140

Phe Gly Gly Gln Gln Ala Ala Lys Met Gly Leu Val Asn Gln Ser Val 145 150 155 160

Pro Leu Ala Glu Leu Arg Ser Val Thr Val Glu Leu Ala Gln Asn Leu 165 170 175

Leu Asp Lys Asn Pro Val Val Leu Arg Ala Ala Lys Ile Gly Phe Lys 180 185 190

Arg Cys Arg Glu Leu Thr Trp Glu Gln Asn Glu Asp Tyr Leu Tyr Ala 195 200 205

Lys Leu Asp Gln Ser Arg Leu Leu Asp Pro Glu Gly Gly Arg Glu Gln 210 215 220

Gly Met Lys Gln Phe Leu Asp Glu Lys Ser Ile Lys Pro Gly Leu Gln 225 230 235 240

Thr Tyr Lys Arg

- (2) INFORMATION FOR SEQ ID NO: 27:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1446 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION:1..1443
 - (D) OTHER INFORMATION:/product= "Vanillin-Dehydrogenase"
 /gene= "vdh"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

ATG TTT CAC GTG CCC CTG CTT ATT GGT GGT AAG CCT TGT TCA GCA TCT Met Phe His Val Pro Leu Leu Ile Gly Gly Lys Pro Cys Ser Ala Ser 245 250 255 260

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							GTG Val 275	96
							GTG Val	144
							AGC Ser	192
							CGT Arg	240
							AAC Asn	288
							GCC Ala 355	336
							GTG Val	384
							CTC Leu	432
							GTT Val	480
							GAG Glu	528
							GCT Ala 435	576
							GAC Asp	624
							CGA Arg	672

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						GGT Gly		720
						GGT Gly		768
						GTC Val		816
						ATG Met		864
						GAA Glu 545		912
						GAT Asp		960
						CGC Arg		1008
						GTC Val		1056
						GAT Asp		1104
						CCT Pro 625		1152
						CTT Leu		1200
						GAC Asp		1248
						TGC Cys		1296
						GGT Gly		1344

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			TAC Tyr													1392
			CGC Arg													1440
ATC Ile 725	TAA															1446
(2)	INF	ORMA'	rion	FOR	SEQ	ID 1	NO: 2	28:								
		(<i>1</i>	SEQUI A) LI B) TY	ENGTI (PE:	H: 48	31 ar no ac	mino cid									
			QUENO LECUI			-		SEQ I	ID NO	D: 28	3:					
Met 1	Phe	His	Val	Pro 5	Leu	Leu	Ile	Gly	Gly 10	Lys	Pro	Cys	Ser	Ala 15	Ser	
Asp	Glu	Arg	Thr 20	Phe	Glu	Arg	Arg	Ser 25	Pro	Leu	Thr	Gly	Glu 30	Val	Val	
Ser	Arg	Val 35	Ala	Ala	Ala	Ser	Leu 40	Glu	Asp	Ala	Asp	Ala 45	Ala	Val	Ala	
Ala	Ala 50	Gln	Ala	Ala	Phe	Pro 55	Glu	Trp	Ala	Ala	Leu 60	Ala	Pro	Ser	Glu	
Arg 65	Arg	Ala	Arg	Leu	Leu 70	Arg	Ala	Ala	Asp	Leu 75	Leu	Glu	Asp	Arg	Ser 80	
Ser	Glu	Phe	Thr	Ala 85	Ala	Ala	ser	Glu	Thr 90		Ala	Ala	Gly	Asn 95	Trp	
Tyr	Gly	Phe	Asn 100	Val	Tyr	Leu	Ala	Ala 105	Gly	Met	Leu	Arg	Glu 110	Ala	Ala	
Ala	Met	Thr 115	Thr	Gln	Ile	Gln	Gly 120	Asp	Val	Ile	Pro	Ser 125	Asn	Val	Pro	
Gly	Ser 130	Phe	Ala	Met	Ala	Val 135	Arg	Gln	Pro	Cys	Gly 140	Val	Val	Leu	Gly	
Ile 145	Ala	Pro	Trp	Asn	Ala 150	Pro	Val	Ile	Leu	Gly 155	Val	Arg	Ala	Val	Ala 160	

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Met	Pro	Leu	Ala	Cys 165	Gly	Asn	Thr	Val	Val 170	Leu	Lys	Ser	Ser	Glu 175	Leu
Ser	Pro	Phe	Thr 180	His	Arg	Leu	Ile	Gly 185	Gln	Val	Leu	His	Asp 190	Ala	Gly
Leu	Gly	Asp 195	Gly	Val	Val	Asn	Val 200	Ile	Ser	Asn	Ala	Pro 205	Gln	Asp	Ala
Pro	Ala 210	Val	Val	Glu	Arg	Leu 215	Ile	Ala	Asn	Pro	Ala 220	Val	Arg	Arg	Val
Asn 225	Phe	Thr	Gly	Ser	Thr 230	His	Val	Gly	Arg	Ile 235	Ile	Gly	Glu	Leu	Ser 240
Ala	Arg	His	Leu	Lys 245	Pro	Ala	Val	Leu	Glu 250	Leu	Gly	Gly	Lys	Ala 255	Pro
Phe	Leu	Val	Leu 260	Asp	Asp	Ala	Asp	Leu 265	Asp	Ala	Ala	Val	Glu 270	Ala	Ala
Ala	Phe	Gly 275	Ala	Tyr	Phe	Asn	Gln 280	Gly	Gln	Ile	Суѕ	Met 285	Ser	Thr	Glu
Arg	Leu 290	Ile	Val	Thr	Ala	Val 295	Ala	Asp	Ala	Phe	Val 300	Glu	Lys	Leu	Ala
Arg 305	Lys	Val	Ala	Thr	Leu 310	Arg	Ala	Gly	Asp	Pro 315	Asn	Asp	Pro	Gln	Ser 320
Val	Leu	Gly	Ser	Leu 325	Ile	Asp	Ala	Asn	Ala 330	Gly	Gln	Arg	Ile	Gln 335	Val
Leu	Val	Asp	Asp 340	Ala	Leu	Ala	Lys	Gly 345	Ala	Arg	Gln	Val	Val 350	Gly	Gly
Gly	Leu	Asp 355	Gly	Ser	Ile	Met	Gln 360	Pro	Met	Leu	Leu	Asp 365	Gln	Val	Thr
Glu	Glu 370	Met	Arg	Leu	Tyr	Arg 375	Glu	Glu	Ser	Phe	Gly 380	Pro	Val	Ala	Val
Val 385	Leu	Arg	Gly	Asp	Gly 390	Asp	Glu	Glu	Leu	Leu 395	Arg	Leu	Ala	Asn	Asp 400
Ser	Glu	Phe	Gly	Leu 405	Ser	Ala	Ala	Ile	Phe 410	Ser	Arg	Asp	Val	Ser 415	Arg
Ala	Met	Glu	Leu 420	Ala	Gln	Arg	Val	Asp 425	Ser	Gly	Ile	Cys	His 430	Ile	Asn
Gly	Pro	Thr 435	Val	His	Asp	Glu	Ala 440	Gln	Met	Pro	Phe	Gly 445	Gly	Val	Lys

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Ser	Ser 450	Gly	Tyr	Gly	Ser	Phe 455	Gly	Ser	Arg	Ala	Ser 460	Ile	Glu	His	Phe	
Thr 465	Gln	Leu	Arg	Trp	Leu 470	Thr	Ile	Gln	Asn	Gly 475	Pro	Arg	His	Tyr	Pro 480	
Ile																
(2)	INF	ORMA!	TION	FOR	SEQ	ID I	NO:	29:								
	(i)	() ()	A) Li B) Ti C) Si	CE CI ENGTI YPE: FRANI OPOLO	H: 1' nucl DEDNI	770] leic Ess:	base acio doul	pai: d	rs							
	(ii)) MO	LECU:	LE T	YPE:	DNA	(gei	nomi	c)							
	(iii)) HYI	POTHI	ETIC	AL: 1	40										
	(iv)) AN'	ri-si	ENSE	: NO											
	(± \delta)	(<i>1</i>	3) LO	AME/I CAT: CHER "Fe	ON:	l1 DRMA: asae	rion ure-0	_	oduct Syntl		se"					
	(xi)	SEÇ	QUEN	CE DI	ESCRI	PTIC	: NC	SEQ I	ID NO	D: 29	9:					
	CGT Arg															48
	CTC Leu															96
	AGG Arg 515															144
	CAC His															192
	GCA Ala															240

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	CAG Gln									288
	TCT Ser									336
	ATC Ile 595									384
	CCT Pro									432
	ATC Ile									480
	AGC Ser									528
_	GCA Ala									576
	ACC Thr 675									624
_	AAT Asn									672
	CCG Pro									720
	CAC His							 		768
	GAC Asp									816
	AGC Ser 755	_								864
_	GAA Glu									912

						GGG Gly		96	0
						CAC His 815		100	8
						ACT Thr		105	6
						TAC Tyr		110	4
						GAT Asp		115	2
						TAC Tyr		120	0
						TAT Tyr 895		124	8
						CAG Gln		129	6
						TCC Ser		1344	4
						CTG Leu		1392	2
						CGT Arg		144(O
						GCC Ala 975		1488	3
						AGT Ser		1536	5

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		Ala	TGG Trp				Trp					Asn				1584
	Gly		GCC Ala			Ile					Leu					1632
			GAT Asp		Gly					Lys					Gln	1680
			TTG Leu 104	Gln					Lys					Tyr		1728
			CAA Gln 0					Asp								1770
(2)		(i) ;	TION SEQUIA) LI S) T O) T O	ENCE ENGTI (PE:	CHAI H: 58 amir	RACTI 39 ar 10 ac	ERIST mino cid	rics								
) MO	DUENC LECUI	LE TY	PE:	prot	cein	SEQ I	ID NO	o: 30):					
Met 1	(xi) MOI	LECUI	CE DE	PE:	prot PTIC	cein ON: S					Arg	Ile	Leu 15	Glu	
1	(xi)) MO) SE Ser	DUENC	CE TY CE DE Glu 5	(PE: ESCRI Ala	prot [PTIC	cein ON: S Leu	Pro	Phe 10	Pro	Gly			15		
1 Arg	(xi) Arg) MO)) SEÇ Ser Glu	LECUI QUENC Leu His	CE TY CE DE Glu 5 Trp	PE: ESCRI Ala Ala Gly	prot PTIC Leu Lys Glu	tein DN: S Leu Thr	Pro Arg 25 Arg	Phe 10 Pro	Pro Glu	Gly Gln Ser	Thr Tyr	Cys 30	15 Val	Ala	
1 Arg Ala	(xi Arg Leu Arg) MOI) SEC Ser Glu Ala 35	LECUI QUENC Leu His 20	CE TY Glu 5 Trp Asn	PE: ESCRI Ala Ala Gly	prot PTIC Leu Lys Glu	Leu Thr Trp 40	Pro Arg 25 Arg	Phe 10 Pro Arg	Pro Glu Ile	Gly Gln Ser	Thr Tyr 45	Cys 30 Ala	15 Val Glu	Ala Met	
Arg Ala Phe	(xi; Arg Leu Arg His) MOS Ser Glu Ala 35	LECUI QUENC Leu His 20 Ala	Glu 5 Trp Asn	PE: ESCRI Ala Ala Gly	prot Leu Lys Glu Ile 55	Thr Trp 40	Pro Arg 25 Arg Gln	Phe 10 Pro Arg	Pro Glu Ile Leu	Gly Gln Ser Leu 60	Thr Tyr 45 Pro	Cys 30 Ala Tyr	15 Val Glu Gly	Ala Met Leu	
Arg Ala Phe Ser 65	(xi Arg Leu Arg His 50) MO!) SE(Ser Glu Ala 35 Asn	LECUI QUENC Leu His 20 Ala	Glu 5 Trp Asn Arg	Ala Ala Gly Ala Leu 70	prot Leu Lys Glu Ile 55	Thr Trp 40 Ala	Pro Arg 25 Arg Gln Val	Phe 10 Pro Arg Ser	Pro Glu Ile Leu Gly 75	Gly Gln Ser Leu 60 Asn	Thr Tyr 45 Pro	Cys 30 Ala Tyr Leu	15 Val Glu Gly Glu	Ala Met Leu His 80	
Arg Ala Phe Ser 65 Leu	Arg Leu Arg His 50 Ala) MO!) SE(Ser Glu Ala 35 Asn Glu	LECUI QUENC Leu His 20 Ala Val	Glu 5 Trp Asn Arg Pro	Ala Ala Gly Ala Leu 70	prot Leu Lys Glu Ile 55 Leu	Thr Trp 40 Ala Ile	Pro Arg 25 Arg Gln Val	Phe 10 Pro Arg Ser Ser	Pro Glu Ile Leu Gly 75	Gly Gln Ser Leu 60 Asn	Thr Tyr 45 Pro Asp	Cys 30 Ala Tyr Leu	15 Val Glu Gly Glu Cys 95	Ala Met Leu His 80 Pro	

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Ala	Pro 130		Gln	Arg	Ala	Ile 135	Glu	Thr	Ile	Leu	Pro 140	Asp	Asp	Val	Pro
Ala 145	Ile	Phe	Thr	Arg	Gly 150	Glu	Leu	Ala	Gly	Arg 155	Arg	Thr	Val	Ser	Phe 160
Asp	Ser	Leu	Leu	Glu 165	Gln	Pro	Gly	Gly	Ile 170		Ala	Asp	Asn	Ala 175	Phe
Ala	Ala	Thr	Gly 180		Asp	Thr	Ile	Ala 185	Lys	Phe	Leu	Phe	Thr 190	Ser	Gly
Ser	Thr	Lys 195	Leu	Pro	Lys	Ala	Val 200	Pro	Thr	Thr	Gln	Arg 205	Met	Leu	Суѕ
Ala	Asn 210	Gln	Gln	Met	Leu	Leu 215	Gln	Thr	Phe	Pro	Val 220	Phe	Gly	Glu	Glu
Pro 225	Pro	Val	Leu	Val	Asp 230	Trp	Leu	Pro	Trp	Asn 235	His	Thr	Phe	Gly	Gly 240
		Asn		245					250					255	
Asp	Asp	Gly	Lys 260	Pro	Thr	Ala	Gln	Gly 265	Phe	Ala	Glu	Thr	Leu 270	Arg	Asn
Leu	Ser	Glu 275	Ile	Ser	Pro	Thr	Ala 280	Tyr	Leu	Thr	Val	Pro 285	Lys	Gly	Trp
Glu	Glu 290	Leu	Val	Gly	Ala	Leu 295	Glu	Arg	Asp	Ser	Thr 300	Leu	Arg	Glu	Arg
Phe 305	Phe	Ala	Arg	Met	Lys 310	Leu	Phe	Phe	Phe	Ala 315	Ala	Ala	Gly	Leu	Ser 320
Gln	Gly	Ile	Trp	Asp 325	Arg	Leu	Asp	Arg	Val 330	Ala	Glu	Gln	His	Cys 335	Gly
Glu	Arg	Ile	Arg 340	Met	Met	Ala	Gly	Leu 345	Gly	Met	Thr	Glu	Thr 350	Ala	Pro
Ser	Cys	Thr 355	Phe	Thr	Thr	Gly	Pro 360	Leu	Ser	Met	Ala	Gly 365	Tyr	Ile	Gly
Leu	Pro 370	Ala	Pro	Gly	Суѕ	Glu 375	Val	Lys	Leu	Val	Pro 380	Val	Asp	Gly	Lys
Leu 385	Glu	Gly	Arg	Phe	His 390	Gly	Pro	His	Val	Met 395	Ser	Gly	Tyr	Trp	Arg 400
Ala	Pro	Glu	Gln	Asn 405	Ala	Gln	Ala	Phe	Asp 410	Glu	Glu	Gly	Tyr	Tyr 415	Cys

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- Ser Gly Asp Ala Ile Lys Leu Ala Asp Pro Ala Asp Pro Gln Lys Gly 420 425 430
- Leu Met Phe Asp Gly Arg Ile Ala Glu Asp Phe Lys Leu Ser Ser Gly 435 440 445
- Val Phe Val Ser Val Gly Pro Leu Arg Thr Arg Ala Val Leu Glu Gly 450 455 460
- Gly Ser Tyr Val Leu Asp Val Val Val Ala Ala Pro Asp Arg Glu Cys 465 470 475 480
- Leu Gly Leu Leu Val Phe Pro Arg Leu Leu Asp Cys Arg Ala Leu Ser 485 490 495
- Gly Leu Gly Lys Glu Ala Ser Asp Ala Glu Val Leu Ala Ser Glu Pro 500 505 510
- Val Arg Ala Trp Phe Ala Asp Trp Leu Lys Arg Leu Asn Arg Glu Ala 515 520 525
- Thr Gly Asn Ala Ser Arg Ile Met Trp Val Gly Leu Leu Asp Thr Pro 530 540
- Pro Ser Ile Asp Lys Gly Glu Val Thr Asp Lys Gly Ser Ile Asn Gln 545 550 555 560
- Arg Ala Val Leu Gln Trp Arg Ser Ala Lys Val Asp Ala Leu Tyr Arg 565 570 575
- Gly Glu Asp Gln Ser Met Leu Arg Asp Glu Ala Thr Leu 580 585
- (2) INFORMATION FOR SEQ ID NO: 31:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1296 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 1..1293
 - (D) OTHER INFORMATION:/product= "beta-Ketothiolase"
 /gene= "aat"

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

ATG Met 590	AGT Ser	TGG Trp	TCA Ser	GGG Gly	GGG Gly 595	Ala	TAC Tyr	TCG Ser	GCG Ala	TTT Phe 600	Ser	GAC Asp	ACT Thr	GCG Ala	TTG Leu 605	48
			GTG Val													96
			CCT Pro 625													144
			TCG Ser													192
			CAA Gln													240
			AGC Ser													288
			GGC Gly													336
ATT Ile	TCC Ser	CAA Gln	GGC Gly 705	GCT Ala	GAT Asp	CAC His	GTG Val	CTG Leu 710	TGT Cys	GTC Val	GCG Ala	GCA Ala	GAG Glu 715	TCC Ser	ATG Met	384
			CCC Pro													432
			GTT Val													480
			GGA Gly													528
			ATC Ile													576
			GCA Ala 785				Gln									624

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										TTA Leu						672
										TTG Leu						720
										TCC Ser 840						768
										AGC Ser						816
										TCG Ser						864
										GTC Val						912
										CGC Arg						960
										TTT Phe 920						1008
										GAA Glu						1056
										GCA Ala						1104
										CTC Leu						1152
										GCA Ala						1200
Gln 990	Gly	Met	Ala	Val	Leu 995	Leu	Glu	Asn	Pro	CAC His 1000	Phe	Gly	Ser	Ser		1248
GCA Ala					Ile)	1293

(2) INFORMATION FOR SEQ ID NO: 32:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 431 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

Met Ser Trp Ser Gly Gly Ala Tyr Ser Ala Phe Ser Asp Thr Ala Leu

1 5 10 15

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Val Ala Ala Val Arg Thr Pro Trp Ile Asp Cys Gly Gly Ala Leu Ser 20 25 30

Leu Val Ser Pro Ile Asp Leu Gly Val Lys Val Ala Arg Glu Val Leu
35 40 45

Met Arg Ala Ser Leu Glu Pro Gln Met Val Asp Ser Val Leu Ala Gly 50 55 60

Ser Met Ala Gln Ala Ser Phe Asp Ala Tyr Leu Leu Pro Arg His Ile 65 70 75 80

Gly Leu Tyr Ser Gly Val Pro Lys Ser Val Pro Ala Leu Gly Val Gln
85 90 95

Arg Ile Cys Gly Thr Gly Phe Glu Leu Leu Arg Gln Ala Gly Glu Gln
100 105 110

Ile Ser Gln Gly Ala Asp His Val Leu Cys Val Ala Ala Glu Ser Met 115 120 125

Ser Arg Asn Pro Ile Ala Ser Tyr Thr His Arg Gly Gly Phe Arg Leu 130 135 140

Gly Ala Pro Val Glu Phe Lys Asp Phe Leu Trp Glu Ala Leu Phe Asp 145 150 155 160

Pro Ala Pro Gly Leu Asp Met Ile Ala Thr Ala Glu Asn Leu Ala Arg 165 170 175

Leu Tyr Gly Ile Thr Arg Gly Glu Ala Asn Ser Tyr Ala Val Ser Ser 180 185 190

Phe Glu Arg Ala Leu Arg Ala Gln Glu Glu Lys Trp Ile Asp Gln Glu 195 200 205

Ile Val Ala Val Thr Asp Glu Gln Phe Asp Leu Glu Gly Tyr Asn Ser 210 215 220

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Arg Ala Ile Glu Leu Pro Arg Lys Ala Lys Leu Leu Ile Val Thr Val Ile Arg Gly Leu Ala Val Phe Glu Ala Leu Ser Arg Leu Lys Pro Val 250 His Ser Gly Gly Val Gln Thr Ala Gly Asn Ser Cys Ala Val Val Asp 265 Gly Ala Ala Ala Leu Val Ala Arg Glu Ser Ser Ala Thr Gln Pro 280 Val Leu Ala Arg Ile Leu Ala Thr Ser Val Val Gly Ile Glu Pro Glu 295 300 His Met Gly Leu Gly Pro Ala Pro Ala Ile Arg Leu Leu Ala Arg 310 315 Ser Asp Leu Ser Leu Arg Asp Ile Asp Leu Phe Glu Ile Asn Glu Ala 325 330 Gln Ala Ala Gln Val Leu Ala Val Gln His Glu Leu Gly Ile Glu His 340 345 350 Ser Lys Leu Asn Ile Trp Gly Gly Ala Ile Ala Leu Gly His Pro Leu Ala Ala Thr Gly Leu Arg Leu Cys Met Thr Leu Ala His Gln Leu Gln 375 Ala Asn Asn Phe Arg Tyr Gly Ile Ala Ser Ala Cys Ile Gly Gly 385 390 395 Gln Gly Met Ala Val Leu Leu Glu Asn Pro His Phe Gly Ser Ser Ser 405 410 Ala Arg Ser Ser Met Ile Asn Arg Val Asp His Tyr Pro Leu Ser

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(2) INFORMATION FOR SEQ ID NO: 33:

420

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1596 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO

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(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION:1..1593
- (D) OTHER INFORMATION:/product= "Chemotaxis-Protein" /gene= "mac"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

ATG Met	ATT Ile	AGT Ser	TTC Phe 435	GCT Ala	CGT Arg	ATG Met	GCA Ala	GAA Glu 440	Ser	TTA Leu	. GGA Gly	GTC Val	CAG Gln 445	GCT Ala	AAA Lys	48
CTT Leu	GCC Ala	CTT Leu 450	GCC Ala	TTC Phe	GCA Ala	CTC Leu	GTA Val 455	TTA Leu	TGT Cys	GTC Val	GGG Gly	CTG Leu 460	ATT Ile	GTT Val	ACC Thr	96
GGC	ACG Thr 465	GGT Gly	TTC Phe	TAC Tyr	AGT Ser	GTA Val 470	CAT His	ACC Thr	TTG Leu	TCA Ser	GGG Gly 475	TTG Leu	GTG Val	GAA Glu	AAG Lys	144
AGC Ser 480	GCG Ala	ATA Ile	GCT Ala	GGT Gly	GAG Glu 485	TTG Leu	CGG Arg	GCG Ala	AAA Lys	ATT Ile 490	CAG Gln	GAA Glu	CTG Leu	AAG Lys	GTT Val 495	192
CTG Leu	GAG Glu	CAG Gln	CGC Arg	GCC Ala 500	TTA Leu	TTC Phe	ATC Ile	GCC Ala	GAT Asp 505	GAA Glu	GGG Gly	TCG Ser	CTG Leu	AAG Lys 510	CAG Gln	240
CGC Arg	TCG Ser	ATC Ile	CTC Leu 515	CTA Leu	AGT Ser	CAG Gln	GTG Val	ATA Ile 520	GCT Ala	GAA Glu	GTT Val	AAT Asn	GAT Asp 525	GCT Ala	ATA Ile	288
GAT Asp	ATT Ile	TTT Phe 530	GAC Asp	TTT Phe	CAG Gln	CGC Arg	GGA Gly 535	CGA Arg	TCT Ser	GAG Glu	TTA Leu	CTT Leu 540	AAA Lys	TTC Phe	GCT Ala	336
GCT Ala	TCT Ser 545	TCG Ser	CGC Arg	GAA Glu	GCA Ala	AGT Ser 550	TAC Tyr	TCC Ser	ATT Ile	GAG Glu	GTC Val 555	GGT Gly	AGT Ser	AAC Asn	GCT Ala	384
GCG Ala 560	GCC Ala	GAT Asp	AAG Lys	TTG Leu	CAG Gln 565	TCG Ser	GGC Gly	GAA Glu	CCA Pro	AGT Ser 570	GAC Asp	GCA Ala	TTG Leu	ATG Met	GTT Val 575	432
GCC Ala	GAT Asp	AAA Lys	AAG Lys	CTG Leu 580	AAT Asn	GTT Val	GAG Glu	TAT Tyr	GAG Glu 585	CAA Gln	TTG Leu	AGT Ser	TCT Ser	GCT Ala 590	GTG Val	480
AAT Asn							Ile									528

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			TAT Tyr													576
ЪÇT	CCT	610 Tat	TCG	ርጥር	ምርር	መጥሮ	615	mcc.	CCT	CDC	mm zi	620	ccc	CCT		CO.4
			Ser													624
			GTG Val													672
			GAC Asp													720
			CGG Arg 675													768
			CGT Arg													816
			CAG Gln													864
			TCT Ser													912
			AGC Ser													960
			cgc Arg 755													1008
			CTC Leu													1056
			AAC Asn													1104
			GCG Ala													1152
			CGT Arg													1200

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	GTT Val								1	.248
	AGG Arg 850								1	.296
	ATG Met								1	.344
	CAA Gln								1	392
	CAA Gln								1	.440
	GCT Ala								1	.488
	GAC Asp 930								1	.536
	CTT Leu								1	.584
TTC Phe 960	CTG Leu	TAG							1	.596

(2) INFORMATION FOR SEQ ID NO: 34:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 531 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

Met Ile Ser Phe Ala Arg Met Ala Glu Ser Leu Gly Val Gln Ala Lys 1 5 10 15

Leu Ala Leu Ala Phe Ala Leu Val Leu Cys Val Gly Leu Ile Val Thr $20 \\ \hspace{1.5cm} 25 \\ \hspace{1.5cm} 30 \\ \hspace{1.5cm}$

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Gly	Thr	Gly 35	Phe	Tyr	Ser	Val	His 40	Thr	Leu	Ser	Gly	Leu 45	Val	Glu	Lys
Ser	Ala 50	Ile	Ala	Gly	Glu	Leu 55	Arg	Ala	Lys	Ile	Gln 60	Glu	Leu	Lys	Val
Leu 65	Glu	Gln	Arg	Ala	Leu 70	Phe	Ile	Ala	Asp	Glu 75	Gly	Ser	Leu	Lys	Gln 80
Arg	Ser	Ile	Leu	Leu 85	Ser	Gln	Val	Ile	Ala 90	Glu	Val	Asn	Asp	Ala 95	Ile
Asp	Ile	Phe	Asp 100	Phe	Gln	Arg	Gly	Arg 105	Ser	Glu	Leu	Leu	Lys 110	Phe	Ala
Ala	Ser	Ser 115	Arg	Glu	Ala	Ser	Tyr 120	Ser	Ile	Glu	Val	Gly 125	Ser	Asn	Ala
Ala	Ala 130	Asp	Lys	Leu	Gln	Ser 135	Gly	Glu	Pro	Ser	Asp 140	Ala	Leu	Met	Val
Ala 145	Asp	Lys	Lys	Leu	Asn 150	Val	Glu	Tyr	Glu	Gln 155	Leu	Ser	Ser	Ala	Val 160
Asn	Ala	Leu	Met	Gly 165	His	Leu	Ile	Glu	Asp 170	Gln	Asn	Glu	Lys	Val 175	Pro
Leu	Ile	Tyr	Туг 180	Met	Leu	Gly	Gly	Val 185	Thr	Leu	Phe	Thr	Met 190	Leu	Met
Ser	Ala	Tyr 195	Ser	Val	Trp	Phe	Ile 200	Ser	Arg	Gln	Leu	Val 205	Pro	Pro	Leu
Lys	Ser 210	Thr	Val	Gln	Leu	Ala 215	Glu	Arg	Ile	Ala	Ser 220	Gly	Asp	Leu	Ala
Asp 225	Val	Gly	Asp	Ser	Arg 230	Arg	Lys	Asp	Glu	Ile 235	Gly	Gln	Leu	Gln	Ser 240
Ala	Thr	Arg	Arg	Met 245	Ala	Ile	Gly	Leu	Arg 250	Asn	Leu	Val	Gly	Asp 255	Ile
G1 *7															
Gly	Gln	Ser	Arg 260	Ala	Gln	Leu	Val	Ser 265	Ser	Ser	Ser	Asp	Leu 270	Ser	Ala
	Gln Cys		260					265					270		
Ile		Ala 275	260 Gln	Ala	Gln	Ile	Asp 280	265 Val	Glu	Cys	Gln	Lys 285	270 Leu	Ser	Val

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Glu Lys Ala Arg Gly Glu Ser Val Val Asn Lys Ala Val Asp Phe 325 330 335

Ile Glu His Leu Ser Gly Asp Met Ala Glu Leu Gly Asp Ala Met Glu 340 345 350

Arg Leu Gln Asn Asp Ser Ala Gln Ile Asn Lys Val Val Asp Val Ile 355 360 365

Lys Ala Val Ala Glu Gln Thr Asn Leu Leu Ala Leu Asn Ala Ala Ile 370 375 380

Glu Ala Arg Ala Gly Glu Gln Gly Arg Gly Phe Ala Val Val Ala 385 390 395 400

Asp Glu Val Arg Ala Leu Ala Met Arg Thr Gln Gln Ser Thr Lys Glu 405 410 415

Ile Glu Arg Leu Val Val Ser Leu Gln Gln Gly Ser Glu Ala Ala Gly 420 425 430

Glu Leu Met Arg Arg Gly Lys Val Arg Thr His Asp Val Val Gly Leu
435 440 445

Ala Gln Gln Ala Ala Arg Arg Ala Thr Arg Asn Tyr Pro Ala Val Ala 450 455 460

Gly Ile Gln Ala Met Asn Tyr Gln Ile Ala Ala Gly Ala Glu Gln Gln 465 470 475 480

Gly Ala Ala Val Val Gln Ile Asn Gln Asn Met Leu Glu Val His Lys 485 490 495

Met Ala Asp Glu Ser Ala Ile Lys Ala Gly Gln Thr Met Lys Ser Ser 500 505 510

Lys Glu Leu Ala His Leu Gly Ser Ala Leu Gln Lys Ser Val Asp Arg 515 520 525

Phe Gln Leu 530

- (2) INFORMATION FOR SEQ ID NO: 35:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 411 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

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- (A) NAME/KEY: CDS
- (B) LOCATION: complement (4..411)
- (D) OTHER INFORMATION:/product=

"Transkriptions-Regulator-Protein" /gene= "trp"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

CTAGCCTAAC TGTTGCGCTT CAGGCTCCGC ATGGATCTTG TGCAGCAGCA ATAGCAATTG 60

TTCACGTTCG TCATCACTCA GCATCGACGT CGCGTCTTGG TCGCTCTGTA CCACGATCTT 120

CTTCAGCTCT TTGAGCTGCG TCTCCCCAGC TTTGCTGAGA AATATCCCAT AGGAACGCTT 180

GTCCGGCTTG CAGCGCACGC GCACAGCAAG GCCGAGCTTC TCGAGCTTGT TCAGCAAGGG 240

AACCAGTTGT GGTGGTTCGA TTGCGAGCAT CCGCGCTAGG TCAGCCTGCA TAAGCCCAGG 300

GCTCGCTTCG ATGATTAGAA GTGCCGACAG CTGCGCCGGG CGTAGGTCAT ATGGCGTCAG 360

GGCTTCAATC AGGCCCTGAG CGAGCTTCAG CTGTGAGCCG GCGTAAGGCA T 411

(2) INFORMATION FOR SEQ ID NO: 36:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 136 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

Met Pro Tyr Ala Gly Ser Gln Leu Lys Leu Ala Gln Gly Leu Ile Glu

1 5 10 15

Ala Leu Thr Pro Tyr Asp Leu Arg Pro Ala Gln Leu Ser Ala Leu Leu 20 25 30

Ile Ile Glu Ala Ser Pro Gly Leu Met Gln Ala Asp Leu Ala Arg Met 35 40 45

Leu Ala Ile Glu Pro Pro Gln Leu Val Pro Leu Leu Asn Lys Leu Glu 50 55 60

Lys Leu Gly Leu Ala Val Arg Val Arg Cys Lys Pro Asp Lys Arg Ser 65 70 75 80

Tyr Gly Ile Phe Leu Ser Lys Ala Gly Glu Thr Gln Leu Lys Glu Leu
85 90 95

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Lys Lys Ile Val Val Gln Ser Asp Gln Asp Ala Thr Ser Met Leu Ser 105 100 Asp Asp Glu Arg Glu Gln Leu Leu Leu Leu His Lys Ile His Ala 115 120 125 Glu Pro Glu Ala Gln Gln Leu Gly (2) INFORMATION FOR SEQ ID NO: 37: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1446 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear (ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 1...1443 (D) OTHER INFORMATION:/product= "Coniferylaldehyd-Dehydrogenase" /gene= "caldh" (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37: ATG AGC ATT CTT GGT TTG AAT GGT GCC CCG GTC GGA GCT GAG CAG CTG 48 Met Ser Ile Leu Gly Leu Asn Gly Ala Pro Val Gly Ala Glu Gln Leu 140 GGC TCG GCT CTT GAT CGC ATG AAG AAG GCG CAC CTG GAG CAG GGG CCT 96 Gly Ser Ala Leu Asp Arg Met Lys Lys Ala His Leu Glu Gln Gly Pro 155 160 GCA AAC TTG GAG CTG CGT CTG AGT AGG CTG GAT CGT GCG ATT GCA ATG 144 Ala Asn Leu Glu Leu Arg Leu Ser Arg Leu Asp Arg Ala Ile Ala Met 175 CTT CTG GAA AAT CGT GAA GCA ATT GCC GAC GCG GTT TCT GCT GAC TTT 192 Leu Leu Glu Asn Arg Glu Ala Ile Ala Asp Ala Val Ser Ala Asp Phe 190 195 GGC AAT CGC AGC CGT GAG CAA ACA CTG CTT TGC GAC ATT GCT GGC TCG 240 Gly Asn Arg Ser Arg Glu Gln Thr Leu Leu Cys Asp Ile Ala Gly Ser 210 205

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GTG Val	GCA Ala	AGC Ser	CTG Leu 220	Lys	GAT Asp	AGC Ser	cgc Arg	GAG Glu 225	His	GTG Val	GCC	AAA Lys	TGG Trp 230	Met	GAG Glu	288
CCC Pro	GAA Glu	CAT His 235	His	AAG Lys	GCG Ala	ATG Met	TTT Phe 240	Pro	. GGG Gly	GCG Ala	GAG Glu	GCA Ala 245	CGC Arg	GTT Val	GAG Glu	336
TTT Phe	CAG Gln 250	Pro	CTG Leu	GGT Gly	GTC Val	GTT Val 255	GGG Gly	GTC Val	ATT Ile	AGT Ser	CCC Pro 260	TGG Trp	AAC Asn	TTC Phe	CCT Pro	384
ATC Ile 265	GTA Val	CTG Leu	GCC Ala	TTT Phe	GGG Gly 270	CCG Pro	CTG Leu	GCC Ala	GGC Gly	ATA Ile 275	TTC Phe	GCA Ala	GCA Ala	GGT Gly	AAT Asn 280	432
						TCC Ser										480
						CGT Arg										528
GTG Val	CTG Leu	GGC Gly 315	GAC Asp	GCT Ala	GAA Glu	GTC Val	GGT Gly 320	GCG Ala	CTG Leu	TTC Phe	AGT Ser	GCT Ala 325	CAG Gln	CCT Pro	TTC Phe	576
						GGC Gly 335										624
CGT Arg 345	GCC Ala	GCG Ala	GCG Ala	GAT Asp	AAC Asn 350	CTA Leu	GTG Val	CCC Pro	GTT Val	ACC Thr 355	CTG Leu	GAA Glu	TTG Leu	GGT Gly	GGC Gly 360	672
AAA Lys	TCG Ser	CCG Pro	GTG Val	ATC Ile 365	GTT Val	TCC Ser	CGC Arg	AGT Ser	GCA Ala 370	GAT Asp	ATG Met	GCG Ala	GAC Asp	GTT Val 375	GCA Ala	720
CAA Gln	CGG Arg	GTG Val	TTG Leu 380	ACG Thr	GTG Val	AAA Lys	ACC Thr	TTC Phe 385	AAT Asn	GCC Ala	GGG Gly	CAA Gln	ATC Ile 390	TGT Cys	CTG Leu	768
						CTG Leu										816
GCC Ala	GAG Glu 410	GCG Ala	ACG Thr	CGC Arg	TTC Phe	GTG Val 415	GCC Ala	GCA Ala	ATG Met	TAT Tyr	ccc Pro 420	TCG Ser	CTT Leu	CTA Leu	GAT Asp	864
AAT Asn 425	CCG Pro	GAT Asp	TAC Tyr	ACG Thr	TCG Ser 430	ATC Ile	ATC Ile	AAT Asn	GCC Ala	CGA Arg 435	AAT Asn	TTC Phe	GAC Asp	CGT Arg	CTG Leu 440	912

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		TAC Tyr								960
		CCT Pro								1008
		ACT Thr 475								1056
		ATC Ile								1104
		GCT Ala								1152
		TTC Phe								1200
		TCG Ser								1248
		ACG Thr 555								1296
		GGC Gly								1344
		CAA Gln								1392
									GAG Glu	1440
TGT Cys	TAG									1446

(2) INFORMATION FOR SEQ ID NO: 38:

(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 481 amino acids

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(B) TYPE: amino acid(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

Met Ser Ile Leu Gly Leu Asn Gly Ala Pro Val Gly Ala Glu Gln Leu 1 5 10 15

Gly Ser Ala Leu Asp Arg Met Lys Lys Ala His Leu Glu Gln Gly Pro 20 25 30

Ala Asn Leu Glu Leu Arg Leu Ser Arg Leu Asp Arg Ala Ile Ala Met 35 40 45

Leu Leu Glu Asn Arg Glu Ala Ile Ala Asp Ala Val Ser Ala Asp Phe 50 55 60

Gly Asn Arg Ser Arg Glu Gln Thr Leu Leu Cys Asp Ile Ala Gly Ser 65 70 75 80

Val Ala Ser Leu Lys Asp Ser Arg Glu His Val Ala Lys Trp Met Glu
85 90 95

Pro Glu His His Lys Ala Met Phe Pro Gly Ala Glu Ala Arg Val Glu 100 105 110

Phe Gln Pro Leu Gly Val Val Gly Val Ile Ser Pro Trp Asn Phe Pro 115 120 125

Ile Val Leu Ala Phe Gly Pro Leu Ala Gly Ile Phe Ala Ala Gly Asn 130 135 140

Arg Ala Met Leu Lys Pro Ser Glu Leu Thr Pro Arg Thr Ser Ala Leu 145 150 155 160

Leu Ala Glu Leu Ile Ala Arg Tyr Phe Asp Glu Thr Glu Leu Thr Thr 165 170 175

Val Leu Gly Asp Ala Glu Val Gly Ala Leu Phe Ser Ala Gln Pro Phe 180 185 190

Asp His Leu Ile Phe Thr Gly Gly Thr Ala Val Ala Lys His Ile Met 195 200 205

Arg Ala Ala Asp Asn Leu Val Pro Val Thr Leu Glu Leu Gly Gly 210 215 220

Lys Ser Pro Val Ile Val Ser Arg Ser Ala Asp Met Ala Asp Val Ala 225 230 235 240

Gln Arg Val Leu Thr Val Lys Thr Phe Asn Ala Gly Gln Ile Cys Leu 245 250 255

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Ala Pro Asp Tyr Val Leu Leu Pro Glu Glu Ser Leu Asp Ser Phe Val 260 265 270

Ala Glu Ala Thr Arg Phe Val Ala Ala Met Tyr Pro Ser Leu Leu Asp 275 280 285

Asn Pro Asp Tyr Thr Ser Ile Ile Asn Ala Arg Asn Phe Asp Arg Leu 290 295 300

His Arg Tyr Leu Thr Asp Ala Gln Ala Lys Gly Gly Arg Val Ile Glu 305 310 315 320

Ile Asn Pro Ala Ala Glu Glu Leu Gly Asp Ser Gly Ile Arg Lys Ile 325 330 335

Ala Pro Thr Leu Ile Val Asn Val Ser Asp Glu Met Leu Val Leu Asn 340 345 350

Glu Glu Ile Phe Gly Pro Leu Leu Pro Ile Lys Thr Tyr Arg Asp Phe 355 360 365

Asp Ser Ala Ile Asp Tyr Val Asn Ser Lys Gln Arg Pro Leu Ala Ser 370 375 380

Tyr Phe Phe Gly Glu Asp Ala Val Glu Arg Glu Gln Val Leu Lys Arg 385 390 395 400

Thr Val Ser Gly Ala Val Val Val Asn Asp Val Met Ser His Val Met 405 410 415

Met Asp Thr Leu Pro Phe Gly Gly Val Gly His Ser Gly Met Gly Ala 420 425 430

Tyr His Gly Ile Tyr Gly Phe Arg Thr Phe Ser His Ala Lys Pro Val 435 440 445

Leu Val Gln Ser Pro Val Gly Glu Ser Asn Leu Ala Met Arg Ala Pro 450 455 460

Tyr Gly Glu Ala Ile His Gly Leu Leu Ser Val Leu Leu Ser Thr Glu 465 470 475 480

Cys

- (2) INFORMATION FOR SEQ ID NO: 39:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1827 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

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(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: complement (4..1827)
- (D) OTHER INFORMATION:/product= "Transkriptions-Aktivator-Protein" /gene= "tap"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

CTATTTGTCT AGTGGTCGGC	GCGAAATTCG	ATAAGAAAGC	TGGGCGCGAG	TGAGGCCGAG	60
CCGGCGGGCA GCTTCCGAGA	CATTGCCTTT	CACCTGGCCC	AGAGCATGGC	TAATCATCGC	120
GTCCTCCACT TCTTGCAGCG	TCATCGCGCT	CAGGTCCTTT	GAGTCAAGCG	GCGAGTCGAT	180
TGTGCTGGTC GGTTTGGAGA	AGGAAGTACT	TGGGCTGCCA	GTTTCCTGTG	GCTGATTATC	240
TTGAGCGGTG GCCAGGATGC	CGCTGGCCCC	AATGGAGAAC	ATCGGTTGAG	TCAGTCGTTC	300
ACCGCTAGTG AAGAGGTGGC	TCACGTCAAT	GGCTCCATCC	TCCGGAGCGC	TGATGACTCC	360
GCGCTCCACC AAATTTTGAA	GCTCCCGGAT	GTTTCCTGGA	AAGTCGTAGC	CAAGCAGGGC	420
ATTGGCTGCA CGTGGAGTGA	ATCCGCTGAC	CACCCGGCTA	TGACGCTGAT	TGAAGCGGTG	480
CAGGAAATAG GTCATCAGGA	GGGGAATGTC	TTCCTTCCTC	TCTCGAAGCG	GCGGGAGGTG	540
GATCGGGTAA ACATTGAGGC	GGAAAAAAAG	GTCCTCGCGG	AACTCGCCGC	GCTGGACGCC	600
TGCGCGAAGA TCGACATTGG	TTGCGGCTAC	CACACGGACG	TCAACCTTGA	GTGTCCTGCT	660
TCCGCCAACC CGTTCGACCT	CCGACTCTTG	CAGGGCGCGA	AGTAACTTCC	CTTGGGCCAC	720
GAGGCTTAGC GTCCCTATCT	CGTCAAGGAA	TAGTGTGCCG	CCCGAAGCGC	GCTCGAACCG	780
TCCTGCTCGA GATTGGGTGG	CGCCGGTAAA	CGCCCCCGT	TCGACGCCGA	ACAACTCGGA	840
CTCCATCAGG GTTTCGGGAA	TACGTGCGCA	ATTGACCGCA	ACAAACGGGC	CGTCGTGTCT	900
GGGGCTGATG CGGTGAAGCA	TGCGGGCGAA	CATCTCCTTG	CCCACACCTG	ATTCACCCGT	960
AAACAGTACC GTCGCCTCCG	TGGGTGCTAC	GCGCTTCAGC	ATGTGGCAGG	CAGCATTGAA	1020
TGCCGAGGAA ATTCCCACCA	TGTCGTGTTC	CGATGCAGTG	CTTGAGTCTG	CGGCGGAGTG	1080
ATGGGGAGTG TTCCTTTGTC	CCTGCTGCGT	TCTTCGTCTC	TGCGGCGTGC	TTGGTTGCCG	1140
ACAAATGGTT GCGCTAAGCG	CCGCCAAGTC	CTCTTCGGCG	TCTTCCCATT	CTTCCGCTGG	1200



CTTGCCGATC	ATGCGGCAGA	TCTGCGAACC	CGTGGAGCGG	CATTCCACCT	CTCGGTAAAG	1260
GATGAGGCGA	CCAACCAGCG	CGGACGTATA	GCCAATGGCA	TAACCCGTCT	GCGTCCAGCA	1320
CGCGGGCTCG	GTGCCGATGC	CGTAGTGCGC	AATATGTTCA	TCATCTTCGC	TCGAATGGTG	1380
CCAGAGGAAT	TCGCCGTAGT	AGGTCCCCAA	ATCCATGTCG	AAGTCGAAGT	GGATCGGCTC	1440
CACGCGTACT	GCGCCTTCCA	GAGAGTGCAA	GTTCGGGCCG	GCGGCAAATA	GGGAGAGCGG	1500
ATCGGCGTTG	CTGAAGCGCT	CCTTCAGAAG	GGCGGCATCT	TTGGCGCCGC	AGTGGTAACC	1560
GGTTCGCAGC	ATGATTCCGC	GGGCGCGGC	GAAGCCCACG	CTTTCAATTA	ATTCGCGTCG	1620
CAATGCACCC	AGTCCGCTGC	TGTGGAGGAG	CAGCATTCGC	GCGCCGTTCA	ACCAGATGCG	1680
ICCATCGCCA	GGGCTGAAAA	GGAGGGATTC	AGTGAGGTCA	TGAAGGGAGG	GGACGGCGCC	1740
TGGCTCCAAT	TGCTCGATGG	CGCCGCGATT	GAGTGTCTTG	GGCGCGGTCT	TGGAGAGTTC	1800
GGCTAGGGAG	ATAAATTTGC	TGGCCAT				1827

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(2) INFORMATION FOR SEQ ID NO: 40:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 608 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

Met Ala Ser Lys Phe Ile Ser Leu Ala Glu Leu Ser Lys Thr Ala Pro 1 5 10 15

Lys Thr Leu Asn Arg Gly Ala Ile Glu Gln Leu Glu Pro Gly Ala Val 20 25 30

Pro Ser Leu His Asp Leu Thr Glu Ser Leu Leu Phe Ser Pro Gly Asp 35 40 45

- Gly Arg Ile Trp Leu Asn Gly Ala Arg Met Leu Leu Leu His Ser Ser 50 55 60
- Gly Leu Gly Ala Leu Arg Arg Glu Leu Ile Glu Ser Val Gly Phe Ala 65 70 75 80
- Arg Ala Arg Gly Ile Met Leu Arg Thr Gly Tyr His Cys Gly Ala Lys
 85 90 95
- Asp Ala Ala Leu Leu Lys Glu Arg Phe Ser Asn Ala Asp Pro Leu Ser 100 105 110

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Leu	Phe	Ala 115	Ala	Gly	Pro	Asn	Leu 120	His	Ser	Leu	Glu	Gly 125	Ala	Val	Arg
Val	Glu 130	Pro	Ile	His	Phe	Asp 135	Phe	Asp	Met	Asp	Leu 140	Gly	Thr	Tyr	Tyr
Gly 145	Glu	Phe	Leu	Trp	His 150	His	Ser	Ser	Glu	Asp 155	Asp	Glu	His	Ile	Ala 160
His	Tyr	Gly	Ile	Gly 165	Thr	Glu	Pro	Ala	Cys 170	Trp	Thr	Gln	Thr	Gly 175	Tyr
Ala	Ile	Gly	Tyr 180	Thr	Ser	Ala	Leu	Val 185	Gly	Arg	Leu	Ile	Leu 190	Tyr	Arg
Glu	Val	Glu 195	Cys	Arg	Ser	Thr	Gly 200	Ser	Gln	Ile	Cys	Arg 205	Met	Ile	Gly
Lys	Pro 210	Ala	Glu	Glu	Trp	Glu 215	Asp	Ala	Glu	Glu	Asp 220	Leu	Ala	Ala	Leu
Ser 225	Ala	Thr	Ile	Cys	Arg 230	Gln	Pro	Ser	Thr	Pro 235	Gln	Arg	Arg	Arg	Thr 240
Gln	Gln	Gly	Gln	Arg 245	Asn	Thr	Pro	His	His 250	Ser	Ala	Ala	Asp	Ser 255	Ser
Thr	Ala	Ser	Glu 260	His	Asp	Met	Val	Gly 265	Ile	Ser	Ser	Ala	Phe 270	Asn	Ala
Ala	Cys	His 275	Met	Leu	Lys	Arg	Val 280	Ala	Pro	Thr	Glu	Ala 285	Thr	Val	Leu
Phe	Thr 290	Gly	Glu	Ser	Gly	Val 295	Gly	Lys	Glu	Met	Phe 300	Ala	Arg	Met	Leu
His 305	Arg	Ile	Ser	Pro	Arg 310	His	Asp	Gly	Pro	Phe 315	Val	Ala	Val	Asn	Cys 320
Ala	Arg	Ile	Pro	Glu 325	Thr	Leu	Met	Glu	Ser 330	Glu	Leu	Phe	Gly	Val 335	Glu
Arg	Gly	Ala	Phe 340	Thr	Gly	Ala	Thr	Gln 345	Ser	Arg	Ala	Gly	Arg 350	Phe	Glu
Arg	Ala	Ser 355	Gly	Gly	Thr	Leu	Phe 360	Leu	Asp	Glu	Ile	Gly 365	Thr	Leu	Ser
Leu	Val 370	Ala	Gln	Gly	Lys	Leu 375	Leu	Arg	Ala	Leu	Gln 380	Glu	Ser	Glu	Val
Glu 385	Arg	Val	Gly	Gly	Ser 390	Arg	Thr	Leu	Lys	Val 395	Asp	Val	Arg	Val	Val 400

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Ala Ala Thr Asn Val Asp Leu Arg Ala Gly Val Gln Arg Gly Glu Phe
405 410 415

Arg Glu Asp Leu Phe Phe Arg Leu Asn Val Tyr Pro Ile His Leu Pro 420 425 430

Pro Leu Arg Glu Arg Lys Glu Asp Ile Pro Leu Leu Met Thr Tyr Phe 435 440 445

Leu His Arg Phe Asn Gln Arg His Ser Arg Val Val Ser Gly Phe Thr 450 455 460

Pro Arg Ala Ala Asn Ala Leu Leu Gly Tyr Asp Phe Pro Gly Asn Ile 465 470 475 480

Arg Glu Leu Gln Asn Leu Val Glu Arg Gly Val Ile Ser Ala Pro Glu 485 490 495

Asp Gly Ala Ile Asp Val Ser His Leu Phe Thr Ser Gly Glu Arg Leu 500 505 510

Thr Gln Pro Met Phe Ser Ile Gly Ala Ser Gly Ile Leu Ala Thr Ala 515 520 525

Gln Asp Asn Gln Pro Gln Glu Thr Gly Ser Pro Ser Thr Ser Phe Ser 530 535 540

Lys Pro Thr Ser Thr Ile Asp Ser Pro Leu Asp Ser Lys Asp Leu Ser 545 550 555 560

Ala Met Thr Leu Gln Glu Val Glu Asp Ala Met Ile Ser His Ala Leu 565 570 575

Gly Gln Val Lys Gly Asn Val Ser Glu Ala Ala Arg Arg Leu Gly Leu 580 585 590

Thr Arg Ala Gln Leu Ser Tyr Arg Ile Ser Arg Arg Pro Leu Asp Lys 595 600 605

(2) INFORMATION FOR SEQ ID NO: 41:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 768 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO

1.

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(ix) FEATURE:

(A) NAME/KEY: CDS(B) LOCATION:1..765

(D) OTHER INFORMATION:/product=

"Coniferylalkohol-Dehydrogenase" /gene= "cadh"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

			AAA Lys 615						48
			CGC Arg						96
			ATG Met						144
			CCT Pro						192
			GGA Gly						240
			GTC Val 695						288
			CTG Leu						336
			CTT Leu						384
								GCA Ala	432
								TTC Phe	480
								TTC Phe	528

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										11,					
		ACG Thr													576
		ATT Ile													624
		GAC Asp												,	672
		GTG Val 835													720
		AAT Asn													765
TAA														•	768
(2)		(E	SEQUE A) LE B) TY		CHAR I: 25 amin	RACTE	RISI ino id	cics:							
	(ii) (xi)	MOI SEÇ		E TY				EQ I	D NC	: 42	: :				

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

Met Gln Leu Thr Asn Lys Lys Ile Val Val Thr Gly Val Ser Ser Gly
1 5 10 15

Ile Gly Ala Glu Thr Ala Arg Val Leu Arg Ser His Gly Ala Thr Val 20 25 30

Ile Gly Val Asp Arg Asn Met Pro Ser Leu Thr Leu Asp Ala Phe Val 35 40 45

Gln Ala Asp Leu Ser His Pro Glu Gly Ile Asp Lys Ala Ile Ser Gln 50 55 60

Leu Pro Glu Lys Ile Asp Gly Leu Cys Asn Ile Ala Gly Val Pro Gly 65 70 75 80

Thr Ala Asp Pro Gln Leu Val Ala Asn Val Asn Tyr Leu Gly Leu Lys
85 90 95

Tyr Leu Thr Glu Ala Val Leu Ser Arg Ile Gln Pro Gly Gly Ser Ile 100 105 110

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Val	Asn	Val 115	Ser	Ser	Val	Leu	Gly 120	Ala	Glu	Trp	Pro	Ala 125	Arg	Leu	Gln
Leu	His 130	Lys	Glu	Leu	Gly	Ser 135	Val	Val	Gly	Phe	Ser 140	Glu	Gly	Gln	Ala
Trp 145	Leu	Lys	Gln	Asn	Pro 150	Val	Ala	Pro	Glu	Phe 155	Cys	Tyr	Gln	Tyr	Phe 160
Lys	Glu	Ala	Leu	Ile 165	Val	Trp	Ser	Gln	Val 170	Gln	Ala	Gln	Glu	Trp 175	Phe
Met	Arg	Thr	Ser 180	Val	Arg	Met	Asn	Cys 185	Ile	Ala	Pro	Gly	Pro 190	Val	Phe
Thr	Pro	Ile 195	Leu	Asn	Glu	Phe	Val 200	Thr	Met	Leu	Gly	Gln 205	Glu	Arg	Thr
Gln	Ala 210	Asp	Ala	His	Arg	Ile 215	Lys	Arg	Pro	Ala	Tyr 220	Ala	Asp	Glu	Val
Ala 225	Ala	Val	Ile	Ala	Phe 230	Met	Cys	Ala	Glu	Glu 235	Ser	Arg	Trp	Ile	Asn 240
Gly	Ile	Asn	Ile	Pro 245	Val	Asp	Gly	Gly	Leu 250	Ala	Ser	Thr	Tyr	Val 255	